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     FILE 'REGISTRY' ENTERED AT 14:31:44 ON 03 JUN 2004
                ACT DEVI643/A
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L1   (          1)SEA FILE=REGISTRY ABB=ON  PLU=ON  SULFO-LC-SPDP/CN
L2   (          1)SEA FILE=REGISTRY ABB=ON  PLU=ON  LC-SPDP/CN
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L4   (          1)SEA FILE=REGISTRY ABB=ON  PLU=ON  SMCC/CN
L5   (          4)SEA FILE=REGISTRY ABB=ON  PLU=ON  MBS/CN
L6   (          1)SEA FILE=REGISTRY ABB=ON  PLU=ON  SMPB/CN
L7   (          6)SEA FILE=REGISTRY ABB=ON  PLU=ON  SMPB ?/CN
L8   (          3)SEA FILE=REGISTRY ABB=ON  PLU=ON  (ADH/CN OR "ADH (ENZYME
L9   (          1)SEA FILE=REGISTRY ABB=ON  PLU=ON  EDAC/CN
L10  (          1)SEA FILE=REGISTRY ABB=ON  PLU=ON  DTSSP/CN
L11            20 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 OR L2 OR L3 OR L4 OR
                  ---------
                   E ADH/CN 5
                   E SMPB/CN
                   E C5A PEPTIDASE/CN 5
L12             4 S E3-E7

     FILE 'HCAPLUS' ENTERED AT 14:36:03 ON 03 JUN 2004
L1   (          1)SEA FILE=REGISTRY ABB=ON  PLU=ON  SULFO-LC-SPDP/CN
L2   (          1)SEA FILE=REGISTRY ABB=ON  PLU=ON  LC-SPDP/CN
L3   (          1)SEA FILE=REGISTRY ABB=ON  PLU=ON  SATA/CN
L4   (          1)SEA FILE=REGISTRY ABB=ON  PLU=ON  SMCC/CN
L5   (          4)SEA FILE=REGISTRY ABB=ON  PLU=ON  MBS/CN
L6   (          1)SEA FILE=REGISTRY ABB=ON  PLU=ON  SMPB/CN
L7   (          6)SEA FILE=REGISTRY ABB=ON  PLU=ON  SMPB ?/CN
L8   (          3)SEA FILE=REGISTRY ABB=ON  PLU=ON  (ADH/CN OR "ADH
                   (ENZYME)"/CN OR "ADH (HORMONE)"/CN)
L9   (          1)SEA FILE=REGISTRY ABB=ON  PLU=ON  EDAC/CN
L10  (          1)SEA FILE=REGISTRY ABB=ON  PLU=ON  DTSSP/CN
L11            20 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 OR L2 OR L3 OR L4
                   OR L5 OR L6 OR L7 OR L8 OR L9 OR L10
L12             4 SEA FILE=REGISTRY ABB=ON  PLU=ON  ("C5A PEPTIDASE"/CN OR
                   "C5A PEPTIDASE (STREPTOCOCCUS AGALACTIAE STRAIN GW GENE
                   SCPB N-TERMINAL FRAGMENT)"/CN OR "C5A PEPTIDASE (STREPTOC
                   OCCUS AGALACTIAE STRAIN I25 GENE SCPB N-TERMINAL
                   FRAGMENT)"/CN OR "C5A PEPTIDASE (STREPTOCOCCUS AGALACTIAE
                    STRAIN I30 GENE SCPB N-TERMINAL FRAGMENT)"/CN OR "C5A
                   PEPTIDASE (STREPTOCOCCUS STRAIN 78-471 GENE SCPB
                   PRECURSOR)"/CN)
L13        129762 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L12 OR TT(S)TETANUS OR
                   TOXIN OR TOXOID OR PNEUMOLYSIN OR FHA OR FILAMENT?(W)(HAE
                   MAGGLUTIN? OR HEMAGGLUTIN?) OR PILI OR PILIN OR OMP OR
                   (SURFACE OR OUTER MEMBRAN?)(W)PROTEIN OR C5A PEPTIDASE
L14         19341 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13 AND (LPS OR LOS OR
                   ENDOTOXIN OR ENDO TOXIN OR LIPOPOLYSACCHARIDE OR
                   LIPOOLIGOSACCHARIDE OR LIPO(W)(POLYSACCHARIDE OR
                   OLIGOSACCHARIDE OR (OLIGO OR POLY)(W)SACCHARIDE) OR
                   (LIPOPOLY OR LIPOOLIGO)(W)SACCHARIDE)
L15          2990 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L14 AND (LINK? OR
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                   CROSSLINK?)
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L17            14 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 AND (L11 OR (LC OR
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LONG CHAIN)(W)SPDP OR SATA OR SATP OR SMCC OR MBS OR IS!ABI OR SMPB OR BANSI OR ADH OR EDAC OR DTSSP OR ADIP?(2W)(DIHYDRAZIDE OR DI HYDRAZIDE))

L18 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L16 AND (SUCCIN?(S)(MALE IMIDO? OR ACETYLTHIOACETATE OR (ACETYL OR AC)(W)(THIOACET ATE OR THIO ACETATE) OR ACETYLTHIO ACETATE) OR (MALEIMIDO BENZ? OR MALEIMIDO BENZ?)(3W)(HYDROXYSUCCIN? OR HYDROXY SUCCIN?) OR MALEIMIDOBENZOYLOXYSUCCIN? OR ETHYL(S)?CARBOD IIMIDE)

L19 14 SEA FILE=HCAPLUS ABB=ON PLU=ON L17 OR L18

L19 ANSWER 1 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 13 Nov 2003
ACCESSION NUMBER: 2003:887632 HCAPLUS
DOCUMENT NUMBER: 139:363588
TITLE: Antigenic **conjugates** of conserved **lipopolysaccharides** of Gram-negative bacteria
INVENTOR(S): Arumugham, Rasappa G.; Fortuna-Nevin, Maria; Apicella, Michael A.; Gibson, Bradford W.
PATENT ASSIGNEE(S): Wyeth Holdings Corporation, USA
SOURCE: U.S., 13 pp., Cont.-in-part of U.S. Provisional Ser. No. 88,364.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6645503	B1	20031111	US 1999-264747	19990309
US 2004052804	A1	20040318	US 2003-643314	20030819

PRIORITY APPLN. INFO.: US 1998-88364P P 19980310
US 1999-264747 A3 19990309

AB The authors disclose **conjugates** comprising a carrier protein **covalently bonded** to the conserved portion of a **lipopolysaccharide** of a Gram-neg. bacterium. The conserved portion of the **lipopolysaccharide** comprises the inner core and lipid A portions of the **lipopolysaccharide**. The **conjugate** elicits a cross-reactive immune response against heterologous strains of the Gram neg. bacterium.

IT **100179-39-3D, C5a Peptidase, conjugates** with Gram-neg. **lipooligosaccharides**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunogenicity of)

IT **1071-93-8, Adipic** acid **dihydrazide 1892-57-5, EDAC 58626-38-3, MBS 64987-85-5, SMCC 76931-93-6, SATA 79886-55-8, SMPB 81069-02-5, DTSSP 158913-22-5, LC-SPDP 169751-10-4,** Sulfo-**LC-SPDP**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(in preparation of **lipooligosaccharide conjugates** of Gram-neg. bacteria)
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 30 Aug 2000
ACCESSION NUMBER: 2000:603707 HCAPLUS
DOCUMENT NUMBER: 133:280268
TITLE: Vibrio cholerae O139 **conjugate** vaccines: synthesis and immunogenicity of V. cholerae O139 capsular polysaccharide **conjugates** with recombinant diphtheria **toxin** mutant in mice
AUTHOR(S): Kossaczka, Zuzana; Shiloach, Joseph; Johnson, Virginia; Taylor, David N.; Finkelstein, Richard A.; Robbins, John B.; Szu, Shousun C.
CORPORATE SOURCE: National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, 20892-2720, USA
SOURCE: Infection and Immunity (2000), 68(9), 5037-5043
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Epidemiol. and exptl. data provide evidence that a critical level of serum IgG antibodies to the surface polysaccharide of Vibrio cholerae O1 (**lipopolysaccharide**) and of Vibrio cholerae O139 (capsular polysaccharide [CPS]) is associated with immunity to the homologous pathogen. The immunogenicity of polysaccharides, especially in infants, may be enhanced by their **covalent** attachment to proteins (**conjugates**). Two synthetic schemes, involving 1-**ethyl**-3-(3-dimethylaminopropyl)**carbodiimide** (EDC) and 1-cyano-4-dimethylaminopyridinium tetrafluoroborate (CDAP) as activating agents, were adapted to prepare four **conjugates** of V. cholerae O139 CPS with the recombinant diphtheria **toxin** mutant, CRMH21G. **Adipic** acid **dihydrazide** was used as a **linker**. When injected s.c. into young outbred mice by a clin. relevant dose and schedule, these **conjugates** elicited serum CPS antibodies of the IgG and IgM classes with vibriocidal activity to strains of capsulated V. cholerae O139. Treatment of these sera with 2-mercaptoethanol (2-ME) reduced, but did not eliminate, their vibriocidal activity. These results indicate that the **conjugates** elicited IgG with vibriocidal activity. **Conjugates** also elicited high levels of serum diphtheria **toxin** IgG. Convalescent sera from 20 cholera patients infected with V. cholerae O139 had vibriocidal titers ranging from 100 to 3,200: absorption with the CPS reduced the vibriocidal titer of all sera to ≤50. Treatment with 2-ME reduced the titers of 17 of 20 patients to ≤50. These data show that, like infection with V. cholerae O1, infection with V. cholerae O139 induces vibriocidal antibodies specific to the surface polysaccharide of this bacterium (CPS) that are mostly of IgM class. Based on these data, clin. trials with the V. cholerae O139 CPS **conjugates** with recombinant

diphtheria **toxin** are planned.

IT **1071-93-8, Adipic** acid **dihydrazide**
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and immunogenicity of Vibrio cholerae O139 capsular polysaccharide **conjugates** with recombinant diphtheria **toxin** mutant **conjugate** vaccines in mice prepared by reaction with)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 22 Sep 1999
ACCESSION NUMBER: 1999:597423 HCAPLUS
DOCUMENT NUMBER: 131:213104
TITLE: Antigenic **conjugates** of conserved **lipopolysaccharides** of gram negative bacteria
INVENTOR(S): Arumugham, Rasappa G.; Fortuna-Nevin, Maria; Apicella, Michael A.; Gibson, Bradford W.
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 941738	A1	19990915	EP 1999-301747	19990309
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2264970	AA	19990910	CA 1999-2264970	19990308
AU 9919540	A1	19990923	AU 1999-19540	19990309
AU 766184	B2	20031009		
JP 11322793	A2	19991124	JP 1999-61354	19990309
BR 9902008	A	20000509	BR 1999-2008	19990309

PRIORITY APPLN. INFO.: US 1998-37529 A 19980310

AB Antigenic **conjugates** are provided which comprise a carrier protein **covalently bonded** to the conserved portion of a **lipopolysaccharide** of a gram neg. bacteria, wherein said conserved portion of the **lipopolysaccharide** comprises the inner core and lipid A portions of said **lipopolysaccharide**, said **conjugate** eliciting a cross reactive immune response against heterologous strains of said gram neg. bacteria. The carrier protein is selected from CRM197, tetanus **toxin**, diphtheria **toxin**, pseudomonas exotoxin A, cholera **toxin**, group A streptococcal **toxin**, **pneumolysin** of Streptococcus pneumoniae, **filamentous hemagglutinin** (**FHA**), **FHA** of Bordetella pertussis, **pili** or **pilins** of Neisseria gonorrhoeae or meningitidis, **outer membrane proteins** of Neisseria meningitidis, **C5A peptidase** of Streptococcus and **surface protein** of Moraxella catarrhalis.

IT **100179-39-3, C5A Peptidase**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(carrier; **conjugates** of conserved **lipopolysaccharides** of gram neg. bacteria and carrier proteins for eliciting cross reactive immune response against heterologous strains of gram neg. bacteria)

IT **1071-93-8, Adipic** acid **dihydrazide**
1892-57-5, EDAC 64987-85-5, SMCC
76931-93-6, SATA 79886-55-8,
Succinimidyl 4-(p-**maleimidophenyl**)butyrate
158913-22-5
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**linker; conjugates** of conserved **lipopolysaccharides** of gram neg. bacteria and carrier proteins for eliciting cross reactive immune response against heterologous strains of gram neg. bacteria)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 01 Oct 1998
ACCESSION NUMBER: 1998:621324 HCAPLUS
DOCUMENT NUMBER: 129:240848
TITLE: Increasing the efficiency of uptake of transforming DNA complexes with polycations using peptides
INVENTOR(S): Hawley-Nelson, Pamela; Lan, Jianqing; Shih, Pojen; Jessee, Joel A.; Ciccarone, Valentina C.; Evans, Krista L.; Schifferli, Kevin P.; Gebeyehu, Guililat
PATENT ASSIGNEE(S): Life Technologies, Inc., USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9840502	A1	19980917	WO 1998-US5232	19980316
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6051429	A	20000418	US 1997-818200	19970314
AU 9865622	A1	19980929	AU 1998-65622	19980316
EP 1007699	A1	20000614	EP 1998-911737	19980316
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,				

PT, IE, FI
JP 2001517939 T2 20011009 JP 1998-539899 19980316
PRIORITY APPLN. INFO.: US 1997-818200 A 19970314
US 1995-477354 B2 19950607
US 1996-658130 A2 19960604
WO 1998-US5232 W 19980316

AB A method of increasing the efficiency of transformation of eukaryotic cells using complexes of nucleic acids with polycations is decribed. The method uses peptide **conjugates** with nucleic acid-**binding** moieties, cationic lipids and dendrimers to complex the DNA. The peptides may be synthetic or derived from a cellular protein and may be further derivatized, e.g. by selective deprotection. The peptide may also be **covalently linked** to the transfection agent (lipid, cationic lipid or dendrimer). Inclusion of peptides or modified-peptides in transfection compns. or **covalent** attachment of peptides to transfection agents increases the efficiency of transfection. Methods for the preparation of transfection compns. and methods of using these transfection compns. as intracellular delivery agents and extracellular targeting agents are also disclosed.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 01 Apr 1998
ACCESSION NUMBER: 1998:189761 HCAPLUS
DOCUMENT NUMBER: 128:312811
TITLE: **Covalent** polymyxin B **conjugate** with human immunoglobulin G as an antiendotoxin reagent
AUTHOR(S): Drabick, Joseph J.; Bhattacharjee, Apurba K.; Hoover, David L.; Siber, George E.; Morales, Vivian E.; Young, Lynnette D.; Brown, Scott L.; Cross, Alan S.
CORPORATE SOURCE: Department of Bacterial Diseases, Walter Reed Army Institute of Research, Washington, DC, 20307-5100, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1998), 42(3), 583-588
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Polymyxin B (PMB) is a cyclic decapeptide antibiotic which also **binds** and neutralizes **endotoxin.** Unfortunately, PMB can be considerably nephrotoxic at clin. utilized doses, thereby limiting its utility as a therapeutic antiendotoxin reagent. We sought to change the pharmacokinetics and toxicity profile of PMB by **covalently linking** it to a human IgG (IgG) carrier. **Conjugates** of PMB with IgG were prepared by **EDAC** [1-**ethyl**-3-(3-dimethylaminopropyl) **carbodiimide**]-mediated amide formation. Anal. by dot ELISA with an anti-PMB monoclonal antibody showed that the purified **conjugate** contained **bound** PMB. The IgG-PMB

conjugate reacted with lipid A and J5 **lipopolysaccharide** in Western blot assays in a manner comparable to that of whole antiserum with anti-lipid A reactivity; unconjugated IgG had no reactivity. The PMB **bound** in the **conjugate** retained its **endotoxin**-neutralizing activity compared to that of unbound PMB as evidenced by its dose-dependent inhibition of tumor necrosis factor release by **endotoxin**-stimulated human monocytes in vitro; unconjugated IgG had no activity. By this assay, the PMB-IgG **conjugate** was determined to have approx. 3.0 μg of **bound** functional PMB per 100 μg of total protein of **conjugate** (five mols. of PMB per IgG mol.). The PMB-IgG **conjugate** was also bactericidal against clin. strains of Escherichia coli, Pseudomonas aeruginosa, and Klebsiella pneumoniae relative to unconjugated IgG with MBCs of <4 μg of **conjugate** per mL for each of the tested strains. The **conjugate** appeared to be nontoxic at the highest doses deliverable and provided statistically significant protection from death to galactosamine-sensitized, **lipopolysaccharide**-challenged mice in a dose-dependent fashion when administered prophylactically 2 h before challenge. However, neither free PMB nor the PMB-IgG **conjugate** could protect mice challenged with **endotoxin** 2 h after administration. This suggests that these reagents can play a role in prophylaxis but not in therapy of sepsis. These expts. demonstrated that the PMB-IgG **conjugate** retains **bound** yet functional PMB as evidenced by its **endotoxin**-neutralizing activity both in vitro and in vivo. Further work is required to define the role that this or related **conjugate** compds. may play in the prophylaxis of **endotoxin**-mediated disease.

IT **1892-57-5DP**, 1-**Ethyl**-3-(3-dimethylaminopropyl) **carbodiimide**], **conjugates** with IgG and polymyxin B
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antibacterial and **endotoxin**-neutralizing activity of polymyxin B **conjugate** with human IgG)

IT **1892-57-5**, 1-**Ethyl**-3-(3-dimethylaminopropyl) **carbodiimide**]
RL: RCT (Reactant); RACT (Reactant or reagent)
(antibacterial and **endotoxin**-neutralizing activity of polymyxin B **conjugate** with human IgG)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 08 May 1996
ACCESSION NUMBER: 1996:269625 HCAPLUS
DOCUMENT NUMBER: 124:340423
TITLE: Preparation and immunogenicity of S flexneri 2a polysaccharide-protein **conjugate**
AUTHOR(S): Xu, Xiaoping; Chen, Zhihua; Su, Xin; Gao, Jieying
CORPORATE SOURCE: Inst. of Microbiology and Epidemiology, Acad. of

Military Med. Sci., Beijing, 100850, Peop. Rep. China
SOURCE: Junshi Yixue Kexueyuan Yuankan (1995), 19(4), 274-7
CODEN: JYKYEL; ISSN: 1000-5501
PUBLISHER: Junshi Yixue Kexueyuan Yuankan Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Polysaccharide (PS) derived from Shigella flexneri 2a **lipopolysaccharide** (**LPS**) was **covalently** coupled to diphtheria **toxoid** (DT) by using **adipic** acid **dihydrazide** as a spacer mol. in the presence of carbodiimide. Immunization of rabbits revealed that the **conjugate** elicited higher F2a **LPS** antibody levels than the PS alone. A clear anti-**LPS** booster effect was induced by the **conjugate**. Anal. of antiserum showed that the antibody was reactive with serogroup A, C, D.

L19 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 03 Aug 1995
ACCESSION NUMBER: 1995:718927 HCAPLUS
DOCUMENT NUMBER: 123:196164
TITLE: Comparative immunogenicity of **conjugates** composed of Escherichia coli O111 O-specific polysaccharide, prepared by treatment with acetic acid or hydrazine, **bound** to tetanus **toxoid** by two synthetic schemes
AUTHOR(S): Gupta, Rajesh K.; Egan, William; Bryla, Dolores A.; Robbins, John B.; Szu, Shousun C.
CORPORATE SOURCE: Nat. Inst. Child Health Human Dev., Nat. Inst. Health, Bethesda, MD, 20892, USA
SOURCE: Infection and Immunity (1995), 63(8), 2805-10
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB E. coli O111, of various H types and virulence factors, causes enteritis throughout the world, especially in young children. This O type is found rarely in healthy individuals. Serum antibodies to the O-specific polysaccharide of O111 **lipopolysaccharide** (**LPS**) protect mice and dogs against infection with this E. coli serotype. The O111 O-specific polysaccharide is composed of a pentasaccharide repeat unit with 2 colitoses **bound** to the C-3 and C-6 of glucose in a trisaccharide backbone; this structure is identical to that of Salmonella adelaide (O35), another enteric pathogen. Nonpyrogenic O111 O-specific polysaccharide was prepared by treatment of its **LPS** with acetic acid (O-SP) or the organic base hydrazine (DeA-**LPS**). The O-SP had a reduced concentration of colitose. These products were derivatized with **adipic** acid **dihydrazide** (**ADH**) or thiolated with N-succinimidyl-3(2-pyridyldithio) propionate (SPDP). The 4 derivs. were **covalently bound** to **tetanus** **toxoid** (**TT**) by carbodiimide-mediated condensation or with SPDP to form **conjugates**. Immunization of BALB/c and general-purpose mice by a clin. acceptable route showed that

DeA-**LPS**-TTADH, of the 4 **conjugates**, elicited the highest level of **LPS** antibodies. Possible reasons to explain this differential immunogenicity between the four **conjugates** are discussed.

L19 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 15 Jun 1995
ACCESSION NUMBER: 1995:612078 HCAPLUS
DOCUMENT NUMBER: 123:81134
TITLE: Synthesis and characterization of a polyvalent Escherichia coli O-polysaccharide-**toxin** A **conjugate** vaccine
AUTHOR(S): Cryz, S. J., Jr.; Que, J. O.; Cross, A. S.; Furer, E.
CORPORATE SOURCE: Swiss Serum and Vaccine Institute, Bern, CH-3001, Switz.
SOURCE: Vaccine (1995), 13(5), 449-53
CODEN: VACCDE; ISSN: 0264-410X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A 12-valent Escherichia coli O-polysaccharide (O-PS)-**toxin** A **conjugate** vaccine was formulated. Nonpyrogenic, low-mol.-weight O-PS was derived from **lipopolysaccharides** (**LPS**) of the following serotypes: 01, 02, 04, 06, 07, 08, 012, 015, 016, 018, 025, and 075. Individual O-PS were **covalently** coupled to Pseudomonas aeruginosa **toxin** A using **adipic** acid **dihydrazide** as a spacer mol. and carbodiimide as a coupling agent. On a weight basis, the final multivalent vaccine was composed of 43% O-PS and 57% **toxin** A. The vaccine was nontoxic and nonpyrogenic in standard animal tests. Immunization of rabbits engendered a marked rise (6-74-fold) in anti-**LPS** IgG antibody titers. When passively transferred to mice, immune rabbit IgG conferred statistically significant protection against a challenge with 9 of the 12 vaccine serotypes. For two serotypes, although the mortality rate declined by ≥50% in the passively immunized vs. the control group, the difference did not reach statistical significance. The degree of protection provided by passively transferred IgG was influenced by both the anti-**LPS** antibody levels in the IgG preparation and the virulence of the challenge strain. Active immunization of mice with either **conjugate** vaccine or killed E. coli whole cells did not confer protection. This was most probably due to the fact that these antigens induced a meagre anti-**LPS** IgG antibody response.

L19 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 02 Oct 1993
ACCESSION NUMBER: 1993:546567 HCAPLUS
DOCUMENT NUMBER: 119:146567
TITLE: Detoxified **lipopolysaccharide**-cholera **toxin conjugate** vaccine for prevention of cholera
INVENTOR(S): Szu, Shousun C.; Robbins, John B.; Gupta, Rajesh K.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA

SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9313797	A2	19930722	WO 1993-US253	19930114
WO 9313797	A3	19931028		
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9334696	A1	19930803	AU 1993-34696	19930114
AU 678549	B2	19970605		
EP 623026	A1	19941109	EP 1993-903428	19930114
R: BE, DE, DK, ES, FR, GB, GR, IE, IT, LU, NL, PT				
JP 07503238	T2	19950406	JP 1993-512624	19930114

PRIORITY APPLN. INFO.: US 1992-821453 19920116
WO 1993-US253 19930114

AB A vaccine against cholera comprises a **conjugate** of detoxified Vibrio cholerae **lipopolysaccharides** (**LPS**) with cholera **toxin** (CT). Detoxification is carried out with hydrazine or by acid hydrolysis. **Conjugation** is carried out by **covalent** attachment, using a bifunctional **linker**, such as N-succinimidyl-3-(2-pyridyldithio)propionate. Alternatively, the detoxified **LPS** can be derivatized for **conjugation** by reaction with **adipic** acid **dihydrazide**, followed by further reaction with 1-**ethyl**-3-(3-dimethylaminopropyl) **carbodiimide**. The **conjugates** have low levels of pyrogen, no toxicity to Chinese hamster ovary cells, and elicit booster responses to vibriocidal and Ct antibodies, when injected s.c. to mice, in saline solution

IT **1071-93-8**, **Adipic** acid **dihydrazide**
1892-57-5D, reaction product with **adipic** acid **dihydrazide**
RL: BIOL (Biological study)
(**linker**, in **conjugation** of detoxified **lipopolysaccharides** with cholera **toxin**, in manufacture of vaccine against cholera)

L19 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 14 May 1993
ACCESSION NUMBER: 1993:198173 HCAPLUS
DOCUMENT NUMBER: 118:198173
TITLE: Escherichia coli O-polysaccharide-protein **conjugate** vaccine
INVENTOR(S): Cryz, Stanley J.; Furer, Emil P.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9303765	A1	19930304	WO 1992-US6531	19920811
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
US 5370872	A	19941206	US 1991-743787	19910812
AU 9224641	A1	19930316	AU 1992-24641	19920811
AU 669854	B2	19960627		
EP 598818	A1	19940601	EP 1992-918016	19920811
EP 598818	B1	20010131		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
JP 06510530	T2	19941124	JP 1993-504334	19920811
JP 2763960	B2	19980611		
AT 198989	E	20010215	AT 1992-918016	19920811
ES 2154263	T3	20010401	ES 1992-918016	19920811
CA 2115564	C	20020122	CA 1992-2115564	19920811
ZA 9206063	A	19930519	ZA 1992-6063	19920812
GR 3035662	T3	20010629	GR 2001-400512	20010329

PRIORITY APPLN. INFO.: US 1991-743787 A 19910812
WO 1992-US6531 A 19920811

AB A polyvalent vaccine composed of nonpyrogenic, nontoxic, immunogenic serotype-specific **lipopolysaccharide** (**LPS**)-based **conjugates**, is prepared by (1) purifying **LPS** from E. coli expressing complete O-polysaccharide side chains, (2) isolating the O-polysaccharide region of the **LPS** mol. by hydrolysis in a dilute AcOH solution and purifying it essentially free of lipid A, and (3) **covalently** coupling lipid A-free O-polysaccharide via at least one OH or CO2H group of the polysaccharide to a carrier protein. Thus, O-polysaccharide was derived from hydrolyzed E. coli **LPS** and **covalently linked** to **toxin** A by using **adipic** acid **dihydrazide** as a spacer mol. The obtained **conjugate** elicited an anti-E. coli **LPS** and an antitoxin A IgG antibody response in both rabbits and humans.

IT **1071-93-8, Adipic** acid **dihydrazide**
RL: BIOL (Biological study)
(spacer agent, in **conjugation** of Escherichia coli polysaccharides with proteins, in preparation of vaccines)

L19 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 13 Apr 1990

ACCESSION NUMBER:	1990:132057 HCAPLUS
DOCUMENT NUMBER:	112:132057
TITLE:	Synthesis and characterization of Escherichia coli O18 O-polysaccharide **conjugate** vaccines
AUTHOR(S):	Cryz, S. J., Jr.; Cross, A. S.; Sadoff, J. C.; Fuerer, E.
CORPORATE SOURCE:	Swiss Serum and Vaccine Inst., Bern, CH-3001, Switz.
SOURCE:	Infection and Immunity (1990), 58(2), 373-7 CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE:	Journal

LANGUAGE: English

AB Nontoxic, serol. reactive O polysaccharide was derived from E. coli O18 **lipopolysaccharide** by acid hydrolysis, extraction with organic solvents, and gel filtration chromatog. Oxidized O polysaccharide was **covalently** coupled to either Pseudomonas aeruginosa **toxin** A or cholera **toxin** by using **adipic** acid **dihydrazide** as a spacer mol. in the presence of carbodiimide. The resulting **conjugates** were composed of approx. equal amts. of O polysaccharide and protein and were nontoxic and nonpyrogenic. Both **conjugates** engendered an IgG antibody response in rabbits that recognized native O18 **lipopolysaccharide**. Such antibody was able to promote the uptake and killing of an E. coli O18 strain bearing the K1 capsule by human polymorphonuclear leukocytes. IgG isolated from the sera of rabbits immunized with either **conjugate** afforded protection against an E. coli O18 challenge when passively transferred to mice.

L19 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 25 Jun 1989
ACCESSION NUMBER: 1989:236989 HCAPLUS
DOCUMENT NUMBER: 110:236989
TITLE: Octavalent Pseudomonas aeruginosa O-polysaccharide-**toxin** A **conjugate** vaccine
AUTHOR(S): Cryz, S. J., Jr.; Sadoff, J. C.; Fuerer, E.
CORPORATE SOURCE: Swiss Serum and Vaccine Inst., Bern, CH-3001, Switz.
SOURCE: Microbial Pathogenesis (1989), 6(1), 75-80
CODEN: MIPAEV; ISSN: 0882-4010
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An octavalent P. aeruginosa **conjugate** vaccine was synthesized by **covalently** coupling the O-polysaacharide (O-PS) moiety derived from **lipopolysaccharides** of Habs serotypes 1, 2, 3, 4, 5, 6, 11 and 12 to **toxin** A. **Adipic** acid **dihydrazide** was used as a spacer mol. to facilitate **conjugation**. The vaccine was composed of 37% O-PS and 63% **toxin** A, devoid of enzymic activity characteristic of **toxin** A, non-toxic for mice and guinea pigs, and nonpyrogenic. The vaccine elicited a significant rise in IgG antibody levels to allserotypes of **lipopolysaccharide** contained in the vaccine and to **toxin** A. Serotypes 6, 10 and 11 were most immunogenic in mice whereas serotypes 1 and 5 engendered the lowest antibody response. Antitoxin A antibody was able to neutralize the cytotoxicity of **toxin** challenge with all P. aeruginosa serotype strains contained in the vaccine.

L19 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 17 May 1986
ACCESSION NUMBER: 1986:166553 HCAPLUS
DOCUMENT NUMBER: 104:166553
TITLE: Pseudomonas aeruginosa immunotype 5 polysaccharide-**toxin** A **conjugate** vaccine
AUTHOR(S): Cryz, S. J., Jr.; Furer, E.; Sadoff, J. C.;

Germanier, R.
CORPORATE SOURCE: Swiss Serum and Vaccine Inst., Bern, 3001, Switz.
SOURCE: Infection and Immunity (1986), 52(1), 161-5
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Polysaccharide (PS) derived from P. aeruginosa immunotype 5 **lipopolysaccharide** was **covalently** coupled to **toxin** A by reductive amination with **adipic** acid **dihydrazide** as a spacer mol. The resulting PS-**toxin** A **conjugate** was composed of 27.5% PS and 72.5% **toxin** A. The **conjugate** was composed of heterogeneous high-mol.-weight species, all of which possessed a mol. weight of >670,000. The **conjugate** was nontoxic for mice and nonpyrogenic at a dose of 50 μg/kg of body weight when i.v. administered to rabbits. Immunization of rabbits with the **conjugate** evoked both an anti-**lipopolysaccharide** IgG and an anti-**toxin** A IgG response. Anti-**conjugate** IgG was capable of neutralizing the cytotoxic effect of **toxin** A. Immunization of mice with the **conjugate** increased the mean LD from 4.5 + 101 P. aeruginosa for control mice to 9.6 + 105 P. aeruginosa for vaccinated mice. Similarly, immunization raised the mean LD for **toxin** A from 0.2 to 4.67 μg per mouse.

L19 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1981:513154 HCAPLUS
DOCUMENT NUMBER: 95:113154
TITLE: Preparation and characterization of detoxified **lipopolysaccharide**-protein **conjugates**
AUTHOR(S): Seid, Robert C., Jr.; Sadoff, Jerald C.
CORPORATE SOURCE: Walter Reed Army Med. Cent., Walter Reed Army Inst. Res., Washington, DC, 20012, USA
SOURCE: Journal of Biological Chemistry (1981), 256(14), 7305-10
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Alkaline treatment of Pseudomonas aeruginosa type 5 **lipopolysaccharide** (**LPS**) resulted in reduced toxicity as measured by both the Limulus amoebocyte assay and the rabbit pyrogenicity test. Chemical anal. of the deacylated **LPS** (D-**LPS**) revealed that ester-**linked** fatty acids were removed whereas the amide-**linked** fatty acids remained intact. The neutral and amino sugar compns. for native **LPS** and D-**LPS** were identical within exptl. error. Antigenic determinants for complement-dependent human opsonic antibody were retained under these deacylation conditions. To enhance its immunogenicity, D-**LPS** was **covalently** coupled to Pseudomonas **pili** and the 1,4-diaminobutyl derivs. of Pseudomonas exotoxin A and tetanus **toxoid**. Quant. amino sugar analyses revealed that 2.6 and 3.2 mol of D-**LPS** were **covalently bound** to aminobutyl Pseudomonas

exotoxin A and aminobutyl tetanus **toxoid**, resp. Gel electrophoresis data indicated ≥1 mol of D- **LPS** **covalently bound**/pilus subunit protein. Initial immunol. data indicated that antibody against D-**LPS** could be induced when the D-**LPS** is **covalently** attached to protein carriers.

IT **1892-57-5**
RL: BIOL (Biological study)
(in **conjugation** of deacylated **lipopolysaccharides** with proteins)

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER, PASCAL, DISSABS, FEDRIP' ENTERED AT 14:51:02 ON 03 JUN 2004)

L20 58 S L19
L21 29 DUP REM L20 (29 DUPLICATES REMOVED)

L21 ANSWER 1 OF 29 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-877151 [81] WPIDS
DOC. NO. CPI: C2003-247714
TITLE: New glycodendrimer useful for treating e.g. sepsis, eczema, rheumatoid arthritis, septic shock, retinal vasculitis and psoriasis comprises carbohydrate moieties **covalently linked** to carboxylic terminated dendrimer.
DERWENT CLASS: B04 C03
INVENTOR(S): DUNCAN, R; GIANASI, E; SHAUNAK, S
PATENT ASSIGNEE(S): (POLY-N) POLYTHERICS LTD
COUNTRY COUNT: 102
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003089010	A1	20031030	(200381)*	EN	63

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003089010	A1	WO 2003-GB1133	20030318

PRIORITY APPLN. INFO: GB 2002-9022 20020419
AN 2003-877151 [81] WPIDS
AB WO2003089010 A UPAB: 20031216
NOVELTY - A glycodendrimer (I) comprising carbohydrate moieties **covalently linked** to carboxylic terminated dendrimer is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) use of (I) in the manufacture of a medicament for the treatment of a disease in which chemokines and cytokines are increased and angiogenesis is increased;

(2) preparation of (I) involving **covalently linking** an amino functionalized carbohydrate to a carboxy terminated dendrimer by using a coupling agent; and

(3) a process for **linking** a molecule e.g. a biologically active molecule, to an anionic dendrimer involving reacting the dendrimer with the biologically active molecule in presence of a coupling agent (e.g. carbodiimide coupling agent).

ACTIVITY - Antiinflammatory; Antibacterial; Immunosuppressive; Dermatological; Antipsoriatic; Vulnerary; Antiarthritic; Antirheumatic; Vasotropic; Antiulcer; Gastrointestinal-Gen.; Cytostatic.

MECHANISM OF ACTION - Angiogenesis inhibitor; Release of chemokine (preferably macrophage inflammatory protein (MIP-1 beta)) and pro-inflammatory cytokine (preferably tumor necrosis factor (TNF- alpha), or interleukin (IL-1 beta)) inhibitor; Synergist.

Single donor peripheral blood mononuclear (PBMN) cells were isolated and resuspended in macrophage growth medium (RPMI), L-glutamine, penicillin, streptomycin and human serum (10%) at a density of 1 multiply 106 cells/ml. The cells were then plated in 12 well tissue culture plates and cultured for 15 minutes at 37 deg. C in 5% carbon dioxide. Dendrimer gen 3.5-glucosamine (test) was then added at a concentration of 150 micro g/ml. The cells were cultured for 30 minutes at 37 deg. C in 5% CO2 and **lipopolysaccharide** (5 ng/ml) was added. Cell free culture supernatants were harvested 24 hours later and assayed for macrophage inflammatory protein-1 beta (MIP-1 beta). The release of MIP-1 beta from single proton PBMN cells for (test) was found to be 10800 pg/ml. Thus, a significant reduction in the cytokine MIP-1 beta release was observed.

USE - In the manufacture of a medicament for the treatment of a disease in which chemokines and cytokines are increased and angiogenesis is increased e.g. for treating severe sepsis, septic shock, systemic inflammatory response associated with sepsis (all caused by liposaccharide from gram negative bacteria or a superantigen **toxin** from a gram positive bacteria), rheumatological disease, eczema, psoriasis, contraction of tissues and excessive scar formation during wound healing, transplant rejection (e.g. corneal, kidney, heart, lung, heart-lung, skin, liver, gut or bone marrow transplant) or graft versus host disease, rheumatoid arthritis, juvenile chronic arthritis, psoriatic arthritis, reactive arthritis occurring after an infection, acute ankylosing spondylitis, arthritis associated with inflammatory bowel disease, Behcet's disease associated with panuveitis and/or retinal vasculitis, inflammatory bowel disease (e.g. Crohn's disease and ulcerative colitis) and a disease associated with metastatic tumor cell growth. Also for treating a tissue or organ (e.g. cornea) (all claimed).

ADVANTAGE - The simultaneous administration of the dendrimer mixture shows synergistic effects with lower doses and less frequent administration resulting in lower toxicity. The glycodendrimers are large molecules and tends to accumulate at the site of inflammation

more rapidly as compared to its accumulation in the normal healthy tissues.
Dwg.0/42

L21 ANSWER 2 OF 29 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-721667 [68] WPIDS
DOC. NO. CPI: C2003-198561
TITLE: Antigenic detoxified bacterial **lipopolysaccharide** useful in vaccines is **linked** to a carrier through complete dephosphorylation of a glycosidically-**linked** phosphate of glycose at the reducing terminus in the lipid A region.
DERWENT CLASS: B04
INVENTOR(S): COX, A; JENNINGS, H; KOGAN, G; MIESZALA, M; MOXON, R; RICHARDS, J C; ZOU, W
PATENT ASSIGNEE(S): (CANA) NAT RES COUNCIL CANADA
COUNTRY COUNT: 102
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003070282	A2	20030828	(200368)*	EN	33
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
AU 2003206532	A1	20030909	(200427)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003070282	A2	WO 2003-CA254	20030224
AU 2003206532	A1	AU 2003-206532	20030224

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003206532	A1 Based on	WO 2003070282

PRIORITY APPLN. INFO: US 2002-358384P 20020222
AN 2003-721667 [68] WPIDS
AB WO2003070282 A UPAB: 20031022
NOVELTY - An antigenic, detoxified bacterial **lipopolysaccharide** (a) is **linked** to a carrier optionally via a **linker** through complete dephosphorylation of a glycosidically-**linked** phosphate or phosphate substituents of glycose at the reducing terminus in the lipid A region.
DETAILED DESCRIPTION - An antigenic, detoxified bacterial **lipopolysaccharide** (a) is **linked** to a carrier

optionally via a **linker** through complete dephosphorylation of a glycosidically-**linked** phosphate or phosphate substituents of glycose at the reducing terminus in the lipid A region. The method involves removing the terminal glycosidic phosphate group to yield a partially or completely dephosphorylated (a) and then **conjugating** (a) to the carrier.

INDEPENDENT CLAIMS are also included for:

(1) An antigenic, detoxified bacterial **lipopolysaccharide**; and

(2) a pharmaceutical composition comprising a **conjugate** vaccine in association with an adjuvant.

ACTIVITY - Antibacterial.

The bactericidal activity of antisera induced in mice by L7-OH,deP-TT **conjugate** against homologous immunotype organism was determined. The **conjugate** showed 40% killing when diluted to 1:10.

MECHANISM OF ACTION - Vaccine.

USE - In polyvalent or multivalent **conjugate** vaccines for combating a Gram-negative or other bacterium (claimed).

ADVANTAGE - The **conjugate** vaccine has optimum presentation of oligosaccharide epitopes having improved immunogenic properties. The vaccines have increased efficacy, reduced side effects, and wide applicability.

Dwg.0/18

L21 ANSWER 3 OF 29 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 2003-455866 [43] WPIDS
DOC. NO. CPI: C2003-121163
TITLE: Immunogenic composition against Neisseria meningitidis, for use as vaccine, has detoxified Neisseria meningitidis **lipooligosaccharide** lacking lacto-N-neotetraose antigen from which primary O-**linked** fatty acid is removed.
DERWENT CLASS: B04 D16
INVENTOR(S): GU, X; TSAI, C
PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6531131	B1	20030311	(200343)*		14

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 6531131	B1 Provisional	US 1999-148021P	19990810
		US 2000-626003	20000726

PRIORITY APPLN. INFO: US 1999-148021P 19990810; US 2000-626003 20000726
AN 2003-455866 [43] WPIDS
AB US 6531131 B UPAB: 20030707
NOVELTY - An immunogenic composition (I) against Neisseria

meningitidis, comprises N.meningitidis **lipooligosaccharide** (**LOS**) which does not contain a lacto-N-neotetraose (LNnT) antigen from which at least one primary O-**linked** fatty acid has been removed to produce detoxified **LOS** (dLOS), and an immunogenic carrier **covalently linked** to it.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) isolated N.meningitidis **LOS** (II) detoxified by removal of at least one primary O-**linked** fatty acid from it, to produce detoxified **LOS** (dLOS) **conjugated** to a carrier;

(2) a composition (III) comprising (I) in a pharmaceutically acceptable carrier;

(3) detoxifying **LOS** from N.meningitidis, by removing at least one primary O-**linked** fatty acid from it, to produce dLOS, and **conjugating** the dLOS to a carrier; and

(4) making (I), by removing at least one primary O-**linked** fatty acid from N.meningitidis **LOS** which does not contain LNnT antigen to produce dLOS, and **covalently binding** the dLOS to an immunogenic carrier.

ACTIVITY - Antiinflammatory; Antibacterial; Immunosuppressive.

MECHANISM OF ACTION - Vaccine (claimed). Immunogenicity of Neisseria meningitidis strain 7880 dLOS-TT **conjugates** was tested in both mice and rabbits. Five week old general purpose mice, ten mice per group, were subcutaneously immunized with 5 micro g (based on **LOS** or dLOS weight) of, dLOS-TT, **LOS** or dLOS plus TT (10 micro g) in 0.2 ml 0.9% NaCl with or without Ribi-700 adjuvant containing 50 micro g monophosphoryl lipid A and 50 micro g synthetic trehalose dimycolate. Mice were injected 3 times at 3 week intervals and bled 14 days after the first injection and 7 days after the second and third injections. New Zealand white rabbits (female, 2-3 kg), 2-3 rabbits per group, were subcutaneously immunized with 50 micro g dLOS, **LOS** or dLOS-TT (carbohydrate weight) in 1 ml 0.9% NaCl with or without Ribi-700 adjuvant. Rabbits were injected twice at one- mount intervals and bled 2 weeks after the first injection and 11-14 days after the second injection. In mice, a mixture of dLOS and TT (unconjugated) did not elicit **LOS** antibodies. dLOS-TT elicited low **LOS** IgG levels after the first injection which increased 3- and 4-fold after the second and third injections, respectively. **LOS** alone elicited low IgG levels after the first injection which increased 2- and 4-fold after the second and third injections, respectively.

USE - (I) is useful for producing antibodies which recognize N.meningitidis in an individual (claimed). (I) is useful as vaccine for prevention of meningitis and septic shock in mammals.

Dwg.0/2

L21 ANSWER 4 OF 29 TOXCENTER COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:283105 TOXCENTER
COPYRIGHT: Copyright 2004 ACS
DOCUMENT NUMBER: CA13924363588N
TITLE: Antigenic **conjugates** of conserved **lipopolysaccharides** of Gram-negative

bacteria
AUTHOR(S): Arumugham, Rasappa G.; Fortuna-Nevin, Maria; Apicella, Michael A.; Gibson, Bradford W.
CORPORATE SOURCE: ASSIGNEE: Wyeth Holdings Corporation
PATENT INFORMATION: US 6645503 B1 11 Nov 2003
SOURCE: (2003) U.S., 13 pp., Cont.-in-part of U.S. Provisional Ser. No. 88,364.
CODEN: USXXAM.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2003:887632
LANGUAGE: English
ENTRY DATE: Entered STN: 20031202
Last Updated on STN: 20031209

AB The authors disclose **conjugates** comprising a carrier protein **covalently bonded** to the conserved portion of a **lipopolysaccharide** of a Gram-neg. bacterium. The conserved portion of the **lipopolysaccharide** comprises the inner core and lipid A portions of the **lipopolysaccharide.** The **conjugate** elicits a cross-reactive immune response against heterologous strains of the Gram neg. bacterium.

L21 ANSWER 5 OF 29 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-163687 [21] WPIDS
CROSS REFERENCE: 2001-272747 [28]
DOC. NO. CPI: C2002-050468
TITLE: **Conjugate** vaccine useful for the treatment of nontypeable Haemophilus influenzae, a causative agent for acute otitis media comprises a **lipooligosaccharide** from which esterified fatty acids have been removed and an immunogenic carrier.
DERWENT CLASS: B04
INVENTOR(S): GU, X; LIM, D J; ROBBINS, J B; TSAI, C
PATENT ASSIGNEE(S): (GUXX-I) GU X; (LIMD-I) LIM D J; (ROBB-I) ROBBINS J B; (TSAI-I) TSAI C; (USSH) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2002001589	A1	20020103	(200221)*		10
US 6607725	B2	20030819	(200356)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2002001589	A1	Provisional	US 1996-16020P	19960423
		Div ex	US 1997-842409	19970423
			US 2001-789017	20010220
US 6607725	B2	Provisional	US 1996-16020P	19960423
		Div ex	US 1997-842409	19970423

US 2001-789017 20010220

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 2002001589	A1 Div ex	US 6207157
US 6607725	B2 Div ex	US 6207157

PRIORITY APPLN. INFO: US 1996-16020P 19960423; US 1997-842409 19970423; US 2001-789017 20010220

AN 2002-163687 [21] WPIDS
CR 2001-272747 [28]
AB US2002001589 A UPAB: 20030903
NOVELTY - A **conjugate** vaccine comprises a **lipooligosaccharide** (DLOS) from which esterified fatty acids have been removed and an immunogenic carrier **covalently linked** to it.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:
(1) isolated nontypeable Haemophilus influenzae (NTHi) **lipooligosaccharide** detoxified by the removal of ester-**linked** fatty acids;
(2) a method of detoxifying **lipooligosaccharide** from NTHi involving the removal of ester-**linked** fatty acids;
(3) a pharmaceutical composition comprising the vaccine **conjugate** in a carrier; and
(4) preparing the **conjugate** vaccine against NTHi involving removing ester-**linked** fatty acids from NTHi **lipooligosaccharide** to produce (dLOS).
ACTIVITY - Auditory; Virucide; Immunostimulant.
MECHANISM OF ACTION - Vaccine.
USE - For the preparation of a **conjugate** vaccine for the treatment of Haemophilus influenzae causing otitis media in a mammal (claimed).
ADVANTAGE - The vaccine is detoxified by removing esterified fatty acids and elicits improved bactericidal response.
Dwg.0/5

L21 ANSWER 6 OF 29 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-432164 [46] WPIDS
CROSS REFERENCE: 1992-150584 [18]; 2001-407313 [43]; 2002-097002 [03]
DOC. NO. CPI: C2001-130688
TITLE: Enhancing presentation of an antigen to an immune cell in a subject to treat chronic infection e.g. AIDS, Hep B comprises administering an antigen-anti-FcgammaRI antibody complex.
DERWENT CLASS: B04 D16
INVENTOR(S): FANGER, M W; GOSSELIN, E J; GUYRE, P M; ROMET-LEMONNE, J L
PATENT ASSIGNEE(S): (MEDA-N) MEDAREX INC
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6258358	B1	20010710	(200146)*		12

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 6258358	B1 CIP of	US 1990-593083	19901005
	Cont of	US 1992-874622	19920427
	Div ex	US 1994-249669	19940526
		US 1995-453500	19950530

PRIORITY APPLN. INFO: US 1992-874622 19920427; US 1990-593083 19901005; US 1994-249669 19940526; US 1995-453500 19950530

AN 2001-432164 [46] WPIDS

CR 1992-150584 [18]; 2001-407313 [43]; 2002-097002 [03]

AB US 6258358 B UPAB: 20020226

NOVELTY - Enhancing (M1) presentation of an antigen (Ag) to an immune cell in a subject, comprising administering, in a pharmacologically acceptable medium, a complex comprising Ag **linked** to an antibody (I) or fragment which **binds** to Fc gamma RI on an Ag-presenting cell without prevention by the natural ligand for the receptor, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for targeting (M2) an antigen to an antigen-presenting cell (APC), comprising contacting the APC with a preformed complex comprising an antibody or fragment which **binds** to Fc gamma RI on an APC without prevention by the natural ligand for the receptor, and antigen that is targeted to the Fc gamma RI receptor on the APC.

ACTIVITY - hepatotrophic; immunostimulant; antiallergic.

MECHANISM OF ACTION - IgG-stimulator.

Monocytes used in the assay were purified from peripheral blood using techniques which minimize contamination with **endotoxins.** Cd4+ T cells used in the assay were isolated following a primary stimulation of donor mononuclear cells with **tetanus toxin.** After three days at 37 deg. C., unbound cells were removed by washing flasks 3 X with Hepes-buffered RPMI-1640 (HRPMI). 40 ml of AIM V were added back to each flask along with 10 units/ml recombinant human interleukin IL-2 and 2.5% autologous serum. After 10 to 14 days total incubation time, T cells were harvested yielding a highly enriched population (90-95%) of CD4+, antigen-specific T cells which minimize non-specific responses and xenogenic responses to mouse immunoglobulin. The mAb-**TT conjugates** used in the assay were made by inducing sulfhydryl groups on **TT** using N-**succinimidyl**-S-**acetyl**-**thioacetate,** and **linking TT** to sulfosuccinimidyl 4-(N **maleimidomethyl**) cyclohexane-I-carboxylate treated (Fab')2 mAb at a 1:1 molar ratio of **TT**:mAb. HIgG anti-**TT** was produced by a hybridoma (SA13) which was obtained from ATCC. Antigen presentation assays were done as follows: 5 X 104 T cells and 5 X 104 monocytes, each in 50 micro l of AIM V medium, were

added to wells of a 96 well microtiter plate. Monocytes were treated with mitomycin C before addition to wells to prevent proliferation of the antigen presenting cells and the few contaminating lymphocytes. Monoclonal antibody ((Fab')2 anti-Fc gamma RI (22.2), Fab anti-Fc gamma RII (IV.3), (Fab')2 anti-Fc gamma RIII (3G8))-**TT conjugates**, or **TT** with or without whole HIgG1 anti-**TT**, was added. Monoclonal antibody 22 (mAb 22) is specific for the high affinity Fc gamma receptor, and its **binding** to the receptor is not blocked by IgG Fc. mAb IV.3 and 3G8 are specific for the ligand **binding** domains of Fc gamma RII and Fc gamma RIII. Following addition of cells and antigen to wells, plates were incubated for 72 hours (h) at 37 deg. C. in a CO2 incubator. After 72 h, (3 H)-thymidine was added in order to detect T cell proliferation. To determine which Fc gamma R types best participate in enhancing antigen presentation, **tetanus toxin** was attached to (Fab')2 anti-Fc gamma RI, Fab anti-Fc gamma RII, or (Fab')2 anti-Fc gamma RIII monoclonal antibodies (mAb). Enhanced presentation of **tetanus toxin** was observed. Anti-Fc gamma RI-**TT** and anti-Fc gamma RII-**TT conjugates** enhanced antigen presentation the greatest (100-fold) as compared to anti-Fc gamma RIII-**TT conjugates** which enhanced antigen presentation the least (10-fold).

USE - M1 is useful for enhancing presentation of an antigen to an immune cell in a subject. M2 is useful for targeting an antigen to an antigen-presenting cell (both claimed). The methods can be used to treat or prevent infectious diseases such as hepatitis B, to neutralize the acute phase of an infection by a pathogenic organism, to stimulate the immune system in instances of chronic infection e.g. AIDS of such an organism, to deplete antigen in the circulation of a subject, and to treat tumors. They can also be used to induce IgG responses against allergens to effect tolerance in the case of IgE-mediated type I hypersensitivity.

ADVANTAGE - The methods reduce the dose of antigen required to obtain a protective or therapeutic immune response or in instances when the host does not respond or responds minimally to the antigen. Although generally desirable, the lowering of effective dose can be especially desirable when the antigen is toxic to the host such as is the case for allergies.

Dwg.0/4

L21 ANSWER 7 OF 29 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER:	2001-272747 [28] WPIDS
CROSS REFERENCE:	2002-163687 [09]
DOC. NO. CPI:	C2001-082667
TITLE:	**Conjugate** vaccine for nontypeable Haemophilus influenzae comprises **lipooligosaccharide** from which esterified fatty acids are removed **conjugated** to immunogenic carrier.
DERWENT CLASS:	B05
INVENTOR(S):	GU, X; LIM, D J; ROBBINS, J B; TSAI, C
PATENT ASSIGNEE(S):	(USSH) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT:	1
PATENT INFORMATION:	

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6207157	B1	20010327	(200128)*		20

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 6207157	B1 Provisional	US 1996-16020P	19960423
		US 1997-842409	19970423

PRIORITY APPLN. INFO: US 1996-16020P 19960423; US 1997-842409 19970423

AN 2001-272747 [28] WPIDS
CR 2002-163687 [09]
AB US 6207157 B UPAB: 20020403
NOVELTY - **Conjugate** vaccine for nontypeable Haemophilus influenzae comprises **lipooligosaccharide** from which esterified fatty acids have been removed from lipid A to form detoxified **lipopolysaccharide** and an immunogenic carrier **covalently linked** to it optionally via a **linker**.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) isolated nontypeable Haemophilus influenzae (NTHi) **lipooligosaccharide** (**LOS**) detoxified by removal of esterified fatty acids from lipid A to form detoxified **lipooligosaccharide** (dLOS) **conjugated** to a carrier and

(2) a pharmaceutical composition comprising the vaccine **conjugate** as above and a carrier.

ACTIVITY - Antibacterial; auditory; respiratory..

MECHANISM OF ACTION - None given.

USE - The vaccine is useful for prevention of otitis media and respiratory infections.

Dwg.0/5

L21 ANSWER 8 OF 29 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-195083 [17] WPIDS
DOC. NO. CPI: C2000-060417
TITLE: New **conjugate** of bacterial O-specific polysaccharide, used in vaccines against infection by hemolytic-uremic Escherichia coli, contains **covalently linked** Shiga **toxin** component.
DERWENT CLASS: B04 D16
INVENTOR(S): KONADU, E; KONADU, Y A; ROBBINS, J B; SZU, S C
PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT: 82
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000004922	A1	20000203	(200017)*	EN	43
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC					

MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI
GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT
LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL
TJ TM TR TT UA UG US UZ VN YU ZW

AU 9885758	A	20000214	(200029)
BR 9815953	A	20010306	(200118)
AU 767047	B	20031030	(200382)#

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000004922	A1	WO 1998-US14976	19980720
AU 9885758	A	AU 1998-85758	19980720
		WO 1998-US14976	19980720
BR 9815953	A	BR 1998-15953	19980720
		WO 1998-US14976	19980720
AU 767047	B	AU 1998-85758	19980720

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9885758	A	Based on	WO 2000004922
BR 9815953	A	Based on	WO 2000004922
AU 767047	B	Previous Publ.	AU 9885758
		Based on	WO 2000004922

PRIORITY APPLN. INFO: WO 1998-US14976 19980720

AN 2000-195083 [17] WPIDS

AB WO 200004922 A UPAB: 20000405

NOVELTY - **Conjugate** (I) comprises an O-specific polysaccharide (II) **covalently bound** to a carrier (III), which is the B-subunit of Shiga **toxin** 1 or 2, or a non-toxic mutant Shiga 1 or 2 holotoxin. (II) is from the Eschericia coli strain O157, forming **conjugate** (Ia), or from E. coli strains O111, O17 or O26, or from Shigella dysenteriae.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a pharmaceutical composition comprising (I) and a carrier;

(2) a vaccine comprising a **conjugate** of (II), from O157, and a carrier protein (III), in a carrier;

(3) a method of inducing serum antibodies which are bacteriostatic or bacteriocidal to E. coli O157, in a mammal, comprising administering (I) in a carrier;

(4) a method of passively immunizing a mammal against E. coli O157 infection, comprising administering the composition of (1) or (2);

(5) a composition comprising antibodies (Ab1) immunoreactive with (II) from O157;

(6) Ab1; and

(7) a composition comprising antibodies (Ab2) immunoreactive with Shiga **toxin** 1 or 2.

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - (I) induce serum antibodies that are

bacteriostatic or bactericidal against E. coli O157. Mice were immunized subcutaneously with 3 doses (14 day intervals) of (II) (from O157)-Shiga **toxin** 1 B subunit **conjugate** (2.5 mu g (II)). Their sera then provided over 99% neutralization of Shiga **toxin** 1 at dilution 1:100, 98% at 1:1000 and 70% at 1:10000, but did not neutralize Shiga 2 **toxin**. The same treatment induced significant levels of antibodies against **lipopolysaccharide**, e.g. titers (in enzyme-**linked** immunosorbant assay) of 0.63 for IgG and 0.14 for IgM.

USE - (Ia) are used as vaccines to protect against infection by E. coli O157 or other strains that cause hemolytic-uremic syndrome. Antibodies raised against (Ia) are useful for passive immunization, for treatment or protection.

ADVANTAGE - (I) induces both bactericidal antibodies against O157 and antibodies against Shiga **toxin**. These antibodies inactivate O157 at the entrance to the jejunum, before infection is established.

Dwg.0/0

L21 ANSWER 9 OF 29 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2000428054 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10948122
TITLE: Vibrio cholerae O139 **conjugate** vaccines: synthesis and immunogenicity of V. cholerae O139 capsular polysaccharide **conjugates** with recombinant diphtheria **toxin** mutant in mice.
AUTHOR: Kossaczka Z; Shiloach J; Johnson V; Taylor D N; Finkelstein R A; Robbins J B; Szu S C
CORPORATE SOURCE: National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland 20892-2720, USA.. kossaczz@mail.nih.gov
SOURCE: Infection and immunity, (2000 Sep) 68 (9) 5037-43. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000922
Last Updated on STN: 20000922
Entered Medline: 20000908

AB Epidemiologic and experimental data provide evidence that a critical level of serum immunoglobulin G (IgG) antibodies to the surface polysaccharide of Vibrio cholerae O1 (**lipopolysaccharide**) and of Vibrio cholerae O139 (capsular polysaccharide [CPS]) is associated with immunity to the homologous pathogen. The immunogenicity of polysaccharides, especially in infants, may be enhanced by their **covalent** attachment to proteins (**conjugates**). Two synthetic schemes, involving 1-**ethyl**-3-(3-dimethylaminopropyl)**carbodiimide** (EDC) and 1-cyano-4-dimethylaminopyridinium tetrafluoroborate (CDAP) as activating agents, were adapted to prepare four **conjugates** of V. cholerae O139 CPS with the recombinant diphtheria **toxin** mutant, CRMH21G. **Adipic** acid **dihydrazide** was used as a **linker**. When injected

subcutaneously into young outbred mice by a clinically relevant dose and schedule, these **conjugates** elicited serum CPS antibodies of the IgG and IgM classes with vibriocidal activity to strains of capsulated V. cholerae O139. Treatment of these sera with 2-mercaptoethanol (2-ME) reduced, but did not eliminate, their vibriocidal activity. These results indicate that the **conjugates** elicited IgG with vibriocidal activity. **Conjugates** also elicited high levels of serum diphtheria **toxin** IgG. Convalescent sera from 20 cholera patients infected with V. cholerae O139 had vibriocidal titers ranging from 100 to 3,200: absorption with the CPS reduced the vibriocidal titer of all sera to < or =50. Treatment with 2-ME reduced the titers of 17 of 20 patients to < or =50. These data show that, like infection with V. cholerae O1, infection with V. cholerae O139 induces vibriocidal antibodies specific to the surface polysaccharide of this bacterium (CPS) that are mostly of IgM class. Based on these data, clinical trials with the V. cholerae O139 CPS **conjugates** with recombinant diphtheria **toxin** are planned.

L21 ANSWER 10 OF 29 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
DUPLICATE 2

ACCESSION NUMBER: 1999-495801 [42] WPIDS
DOC. NO. CPI: C1999-145508
TITLE: New antigenic **conjugates** from bacteria, useful as vaccines.
DERWENT CLASS: B04 D16
INVENTOR(S): APICELLA, M A; ARUMUGHAM, R G; FORTUNA-NEVIN, M; GIBSON, B W
PATENT ASSIGNEE(S): (AMHP) WYETH HOLDINGS CORP; (AMCY) AMERICAN CYANAMID CO
COUNTRY COUNT: 31
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 941738	A1	19990915	(199942)*	EN	17
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
AU 9919540	A	19990923	(199951)		
CA 2264970	A1	19990910	(200006)	EN	
JP 11322793	A	19991124	(200006)		18
BR 9902008	A	20000509	(200033)		
KR 99077705	A	19991025	(200052)		
AU 766184	B	20031009	(200373)		
US 6645503	B1	20031111	(200382)#		
US 2004052804	A1	20040318	(200421)#		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 941738	A1	EP 1999-301747	19990309
AU 9919540	A	AU 1999-19540	19990309
CA 2264970	A1	CA 1999-2264970	19990308
JP 11322793	A	JP 1999-61354	19990309

BR 9902008	A	BR 1999-2008	19990309
KR 99077705	A	KR 1999-7668	19990309
AU 766184	B	AU 1999-19540	19990309
US 6645503	B1 Provisional	US 1998-88364P	19980310
		US 1999-264747	19990309
US 2004052804	A1 Provisional Div ex	US 1998-88364P	19980310
		US 1999-264747	19990309
		US 2003-643314	20030819

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 766184	B Previous Publ.	AU 9919540
US 2004052804	A1 Div ex	US 6645503

PRIORITY APPLN. INFO: US 1998-37529 19980310; US 1999-264747 19990309; US 2003-643314 20030819

AN 1999-495801 [42] WPIDS

AB EP 941738 A UPAB: 19991014

NOVELTY - An antigenic **conjugate** (I) comprising a carrier protein **covalently bonded** to the conserved portion of a **lipopolysaccharide** (**LPS**) of a gram negative bacteria is new. The conserved portion comprises the inner core and lipid A regions of the **LPS** and the **conjugate** elicits a cross reactive immune response against heterologous strains of gram negative bacteria.

ACTIVITY - None given.

MECHANISM OF ACTION - Vaccine.

USE - (I) may be administered to patients as a prophylactic vaccine against Neisseria gonorrhoeae, Haemophilus influenzae, Haemophilus ducreyi, Helicobacter pylori, Escherichia coli, Chlamydia, Salmonella, Salmonella typhimurium, Salmonella minnesota, Proteus mirabilis, Pseudomonas aeruginosa, Moraxella catarrhalis, Bordetella pertussis, Shigella, Klebsiella and Vibrio cholerae, especially Neisseria meningitidis which produce **LPS** (claimed). These vaccines may be used to prevent bacterial sepsis. Antibodies generated by these vaccines may be used to examine whether an infection has been caused by an **LPS**-producing organism by testing blood samples, body fluids or biopsy materials of infected individuals. These antibodies may also be directly administered to patients as prophylactic agents against the bacteria listed above.

ADVANTAGE - (I) induces a cross-reactive and cross-functional antibody response against heterologous strains of gram negative bacteria. In contrast prior art **LPS** vaccines were restricted in the number of strains they protected against.

Dwg.0/4

L21 ANSWER 11 OF 29 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 1999-444322 [37] WPIDS

DOC. NO. CPI: C1999-130893

TITLE: Detoxified **lipooligosaccharide**-based vaccine for prevention of Moraxella catarrhalis infections in mammals.

DERWENT CLASS: B04 D16
INVENTOR(S): GU, X; ROBBINS, J B
PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT: 85
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9936086	A1	19990722	(199937)*	EN	60
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9922212	A	19990802	(199954)		
BR 9906902	A	20001017	(200056)		
EP 1047447	A1	20001102	(200056)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
CN 1288384	A	20010321	(200137)		
KR 2001034124	A	20010425	(200164)		
MX 2000006678	A1	20010201	(200168)		
JP 2002509115	W	20020326	(200236)		66
US 6685949	B1	20040203	(200413)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9936086	A1		WO 1999-US590	19990112
AU 9922212	A		AU 1999-22212	19990112
BR 9906902	A		BR 1999-6902	19990112
			WO 1999-US590	19990112
EP 1047447	A1		EP 1999-902170	19990112
			WO 1999-US590	19990112
CN 1288384	A		CN 1999-802142	19990112
KR 2001034124	A		KR 2000-707737	20000713
MX 2000006678	A1		MX 2000-6678	20000706
JP 2002509115	W		WO 1999-US590	19990112
			JP 2000-539859	19990112
US 6685949	B1	Provisional	US 1998-71483P	19980113
		Cont of	WO 1999-US590	19990112
			US 2000-610034	20000705

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9922212	A	Based on	WO 9936086
BR 9906902	A	Based on	WO 9936086
EP 1047447	A1	Based on	WO 9936086
JP 2002509115	W	Based on	WO 9936086

PRIORITY APPLN. INFO: US 1998-71483P 19980113; US 2000-610034 20000705
AN 1999-444322 [37] WPIDS

Searcher : Shears 571-272-2528

AB WO 9936086 A UPAB: 19990914
NOVELTY - A **lipooligosaccharide** (**LOS**) isolated from Moraxella catarrhalis and detoxified by removal of ester-**linked** fatty acids to produce detoxified **LOS** (dLOS) or treated to remove lipid A to produce oligosaccharide (OS) is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for a **conjugate** vaccine for M. catarrhalis comprising dLOS or OS, and a **covalently linked** immunogenic carrier as above; methods of detoxifying **LOS** isolated from M. catarrhalis, by removal of ester-**linked** fatty acids; methods of making a **conjugate** vaccine as above.
ACTIVITY - Immunoprotective; Auditory; Antibacterial.
MECHANISM OF ACTION - Vaccine.
USE - The methods are useful for isolation of detoxified **lipooligosaccharide** or oligosaccharide from M. catarrhalis. The detoxified **lipooligosaccharide** or oligosaccharide are useful in **conjugate** vaccines. The vaccine is useful for protection against M. catarrhalis which causes otitis media and respiratory infections.
ADVANTAGE - The invention provides a detoxified **lipooligosaccharide** from M. catarrhalis, the major virulence factor for pathogenesis of bacterial infections. When tested by the standard Limulus amebocyte lysate assay, the isolated **LOS** showed 2 x 104 EU/ mu g, whereas the dLOS showed 1 EU/ mu g, representing a 20000-fold reduction of toxicity.
Dwg.0/3

L21 ANSWER 12 OF 29 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 3

ACCESSION NUMBER: 1998:176999 BIOSIS
DOCUMENT NUMBER: PREV199800176999
TITLE: **Covalent** polymyxin B **conjugate** with human immunoglobulin G as an antiendotoxin reagent.
AUTHOR(S): Drabick, Joseph J. [Reprint author]; Bhattacharjee, Apurba K.; Hoover, David L.; Siber, George E.; Morales, Vivian E.; Young, Lynnette D.; Brown, Scott L.; Cross, Alan S.
CORPORATE SOURCE: Hematology/Oncology Service, Walter Reed Army Med. Cent., Washington, DC 20307-5100, USA
SOURCE: Antimicrobial Agents and Chemotherapy, (March, 1998) Vol. 42, No. 3, pp. 583-588. print.
CODEN: AMACCQ. ISSN: 0066-4804.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Apr 1998
Last Updated on STN: 12 Aug 1998

AB Polymyxin B (PMB) is a cyclic decapeptide antibiotic which also **binds** and neutralizes **endotoxin**. Unfortunately, PMB can be considerably nephrotoxic at clinically utilized doses, thereby limiting its utility as a therapeutic antiendotoxin reagent. We sought to change the pharmacokinetics and toxicity profile of PMB by **covalently linking** it to a human immunoglobulin G (IgG) carrier. **Conjugates** of PMB with IgG were prepared by **EDAC** (1-**ethyl**

-3-(3-dimethylaminopropyl) **carbodiimide**)-mediated amide formation. Analysis by dot enzyme-**linked** immunosorbent assay with an anti-PMB monoclonal antibody showed that the purified **conjugate** contained **bound** PMB. The IgG-PMB **conjugate** reacted with lipid A and J5 **lipopolysaccharide** in Western blot assays in a manner comparable to that of whole antiserum with anti-lipid A reactivity; unconjugated IgG had no reactivity. The PMB **bound** in the **conjugate** retained its **endotoxin**-neutralizing activity compared to that of unbound PMB as evidenced by its dose-dependent inhibition of tumor necrosis factor release by **endotoxin**-stimulated human monocytes in vitro; unconjugated IgG had no activity. By this assay, the PMB-IgG **conjugate** was determined to have approximately 3.0 mug of **bound** functional PMB per 100 mug of total protein of **conjugate** (five molecules of PMB per IgG molecule). The PMB-IgG **conjugate** was also bactericidal against clinical strains of Escherichia coli, Pseudomonas aeruginosa, and Klebsiella pneumoniae relative to unconjugated IgG with MBCs of <4 mug of **conjugate** per ml for each of the tested strains. The **conjugate** appeared to be nontoxic at the highest doses deliverable and provided statistically significant protection from death to galactosamine-sensitized, **lipopolysaccharide** -challenged mice in a dose-dependent fashion when administered prophylactically 2 h before challenge. However, neither free PMB nor the PMB-IgG **conjugate** could protect mice challenged with **endotoxin** 2 h after administration. This suggests that these reagents can play a role in prophylaxis but not in therapy of sepsis. These experiments demonstrated that the PMB-IgG **conjugate** retains **bound** yet functional PMB as evidenced by its **endotoxin**-neutralizing activity both in vitro and in vivo. Further work is required to define the role that this or related **conjugate** compounds may play in the prophylaxis of **endotoxin**-mediated disease.

L21 ANSWER 13 OF 29 MEDLINE on STN
ACCESSION NUMBER: 97190160 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9038315
TITLE: Bactericidal antibody responses of juvenile rhesus monkeys immunized with group B Neisseria meningitidis capsular polysaccharide-protein **conjugate** vaccines.
AUTHOR: Zollinger W D; Moran E E; Devi S J; Frasch C E
CORPORATE SOURCE: Department of Bacterial Diseases, Walter Reed Army Institute of Research, Washington, D.C. 20307-5100, USA.
SOURCE: Infection and immunity, (1997 Mar) 65 (3) 1053-60. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970321
Last Updated on STN: 19970321
Entered Medline: 19970313

Searcher : Shears 571-272-2528

AB Reports on the bactericidal activities of antibodies to group B Neisseria meningitidis capsular polysaccharide (B PS) are conflicting. Using three different complement sources, we analyzed the bactericidal activities of sera of juvenile rhesus monkeys immunized with five **conjugate** vaccines of B PS synthesized by different schemes, an Escherichia coli K92 **conjugate**, and a noncovalent complex of B PS with group B meningococcal outer membrane vesicles (B+OMV) (S. J. N. Devi, W. D. Zollinger, P. J. Snoy, J. Y. Tai, P. Costantini, F. Norelli, R. Rappuoli, and C. E. Frasch, Infect. Immun. 65:1045-1052, 1997). With rabbit complement, nearly all preimmune sera showed relatively high bactericidal titers, and all vaccines, except the K92 **conjugate**, induced a fourfold or greater increase in bactericidal titers in most of the monkeys vaccinated. In contrast, with human complement, most prevaccination sera showed no bactericidal activity and in most of the vaccine groups, little or no increase in bactericidal titer was observed. However, the **covalent conjugation** of P BS and OMV (B-OMV) administered with and without the Ribi adjuvant induced relatively high bactericidal titers which persisted up to 30 weeks. An analysis of the specificities of bactericidal antibodies revealed that absorption with E. coli K1 cells did not change the bactericidal titer with human complement but reduced the titers observed with the rabbit and monkey complements. A significant increase in anti-**lipopolysaccharide** (**LPS**) antibodies was elicited by the B-OMV **conjugates**, and nearly all of the bactericidal activity with human complement could be inhibited with the purified group B meningococcal L3,7,8 **LPS**. B-OMV **covalently** coupled via **adipic** acid **dihydrazide** elicited significantly elevated levels (P < or = 0.02) of anti-OMV antibodies compared to those of the noncovalently complexed B+OMV. An initial small-scale evaluation of B PS **conjugates** in adult human males appears feasible, with careful monitoring, to settle the inconsistent reports of the importance of source of complement in eliciting bacteriolysis. Subsequent analysis of resultant human antibodies for bacteriolysis, opsonophagocytosis, and protective efficacy in animal models may be the first step toward answering safety- and efficacy-related concerns about B PS **conjugate** vaccines.

L21 ANSWER 14 OF 29 MEDLINE on STN DUPLICATE 4

ACCESSION NUMBER: 95347786 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7542631

TITLE: Comparative immunogenicity of **conjugates** composed of Escherichia coli O111 O-specific polysaccharide, prepared by treatment with acetic acid or hydrazine, **bound** to tetanus **toxoid** by two synthetic schemes.

AUTHOR: Gupta R K; Egan W; Bryla D A; Robbins J B; Szu S C
CORPORATE SOURCE: National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland 20892, USA.

SOURCE: Infection and immunity, (1995 Aug) 63 (8) 2805-10. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950911
Last Updated on STN: 19960129
Entered Medline: 19950825

AB Escherichia coli O111, of various H types and virulence factors, causes enteritis throughout the world, especially in young children. This O type is found rarely in healthy individuals. Serum antibodies to the O-specific polysaccharide of O111 **lipopolysaccharide** (**LPS**) protect mice and dogs against infection with this E. coli serotype. The O111 O-specific polysaccharide is composed of a pentasaccharide repeat unit with two colitoses **bound** to the C-3 and C-6 of glucose in a trisaccharide backbone; this structure is identical to that of Salmonella adelaide (O35), another enteric pathogen. Nonpyrogenic O111 O-specific polysaccharide was prepared by treatment of its **LPS** with acetic acid (O-SP) or the organic base hydrazine (DeA-**LPS**). The O-SP had a reduced concentration of colitose. These products were derivatized with **adipic** acid **dihydrazide** (**ADH**) or thiolated with N-succinimidyl-3(2-pyridyldithio) propionate (SPDP). The four derivatives were **covalently bound** to **tetanus toxoid** (**TT**) by carbodiimide-mediated condensation or with SPDP to form **conjugates**. Immunization of BALB/c and general-purpose mice by a clinically acceptable route showed that DeA-**LPS** -TTADH, of the four **conjugates**, elicited the highest level of **LPS** antibodies. Possible reasons to explain this differential immunogenicity between the four **conjugates** are discussed.

L21 ANSWER 15 OF 29 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 95366223 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7639013
TITLE: Synthesis and characterization of a polyvalent Escherichia coli O-polysaccharide-**toxin** A **conjugate** vaccine.
AUTHOR: Cryz S J Jr; Que J O; Cross A S; Furer E
CORPORATE SOURCE: Swiss Serum and Vaccine Institute, Berne.
SOURCE: Vaccine, (1995 Apr) 13 (5) 449-53.
Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199509
ENTRY DATE: Entered STN: 19950921
Last Updated on STN: 20020420
Entered Medline: 19950914

AB A 12-valent Escherichia coli O-polysaccharide (O-PS)-**toxin** A **conjugate** vaccine was formulated. Nonpyrogenic, low-molecular-weight O-PS was derived from **lipopolysaccharides** (**LPS**) of the following serotypes: O1,O2,O4,O6,O7,O8,O12, O15,O16,O18,O25, and O75. Individual O-PS were **covalently** coupled to Pseudomonas

aeruginosa **toxin** A using **adipic** acid **dihydrazide** as a spacer molecule and carbodiimide as a coupling agent. On a weight basis, the final multivalent vaccine was composed of 43% O-PS and 57% **toxin** A. The vaccine was nontoxic nad nonpyrogenic in anti-**LPS** immunoglobulin G (IgG) antibody titers. When passively transferred to mice, immune rabbit IgG conferred statistically significant ($p < 0.05$) protection against a challenge with 9 of the 12 vaccine serotypes. For two serotypes, although the mortality rate declined by > or 50% in the passively immunized versus the control group, the difference did not reach statistical significance. The degree of protection provided by passively transferred IgG was influenced by both the anti-**LPS** antibody levels in the IgG preparation and the virulence of the challenge strain. Active immunization of mice with either **conjugate** vaccine or killed E. coli whole cells did not confer protection. This was most probably due to the fact that these antigens induced a meagre anti-**LPS** IgG antibody response.

L21 ANSWER 16 OF 29 TOXCENTER COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:155886 TOXCENTER
COPYRIGHT: Copyright 2004 ACS
DOCUMENT NUMBER: CA12425340423F
TITLE: Preparation and immunogenicity of S flexneri 2a polysaccharide-protein **conjugate**
AUTHOR(S): Xu, Xiaoping; Chen, Zhihua; Su, Xin; Gao, Jieying
CORPORATE SOURCE: Inst. of Microbiology and Epidemiology, Acad. of Military Med. Sci., Beijing, 100850, Peop. Rep. China.
SOURCE: Junshi Yixue Kexueyuan Yuankan, (1995) Vol. 19, No. 4, pp. 274-7.
CODEN: JYKYEL. ISSN: 1000-5501.
COUNTRY: CHINA
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1996:269625
LANGUAGE: Chinese
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020903

AB Polysaccharide (PS) derived from Shigella flexneri 2a **lipopolysaccharide** (**LPS**) was **covalently** coupled to diphtheria **toxoid** (DT) by using **adipic** acid **dihydrazide** as a spacer mol. in the presence of carbodiimide. Immunization of rabbits revealed that the **conjugate** elicited higher F2a **LPS** antibody levels than the PS alone. A clear anti-**LPS** booster effect was induced by the **conjugate**. Anal. of antiserum showed that the antibody was reactive with serogroup A, C, D.

L21 ANSWER 17 OF 29 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
DUPLICATE 6
ACCESSION NUMBER: 1993-242913 [30] WPIDS
DOC. NO. CPI: C1993-108226
TITLE: Vaccine comprising bacterial **lipo-polysaccharide conjugated** to a protein - for immunisation against cholera.

DERWENT CLASS: B04 D16
INVENTOR(S): GUPTA, R K; ROBBINS, J B; SZU, S C
PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES; (USSH) US SEC DEPT HEALTH; (USSH) US DEPT HEALTH & HUMAN SERVICE
COUNTRY COUNT: 19
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9313797	A2	19930722	(199330)*	EN	40
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: AU CA JP					
AU 9334696	A	19930803	(199348)		
EP 623026	A1	19941109	(199443)	EN	
R: BE DE DK ES FR GB GR IE IT LU NL PT					
JP 07503238	W	19950406	(199522)		
AU 678549	B	19970605	(199731)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9313797	A2	WO 1993-US253	19930114
AU 9334696	A	AU 1993-34696	19930114
		WO 1993-US253	19930114
EP 623026	A1	EP 1993-903428	19930114
		WO 1993-US253	19930114
JP 07503238	W	JP 1993-512624	19930114
		WO 1993-US253	19930114
AU 678549	B	AU 1993-34696	19930114

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9334696	A	Based on	WO 9313797
EP 623026	A1	Based on	WO 9313797
JP 07503238	W	Based on	WO 9313797
AU 678549	B	Previous Publ.	AU 9334696
		Based on	WO 9313797

PRIORITY APPLN. INFO: US 1992-821453 19920116
AN 1993-242913 [30] WPIDS
AB WO 9313797 A UPAB: 19931118
Vaccine comprises (1) purified isolated bacterial **lipopolysaccharide** (**LPS**) which has been detoxified so that it has low pyrogenicity in mammals and (2) an acceptable carrier.

Also new are (1) **conjugates** (C) of such **LPS** **covalently** attached (via a bifunctional **linker**) to a protein (I) isolated from (or secreted by) a bacterium and (2) aggregates of (C) in which components reacted with **adipic** acid **dihydrazide** (II) as bifunctional **linker** are reacted further with 1-**ethyl**-3-(3-dimethylamino propyl) **carbodiimide** (**EDAC**). Pref. **LPS** is

detoxified by reaction with hydrazine or by acid hydrolysis. The vaccines can be formulated with a second vaccine, e.g. diphtheria/tetanus/pertussis.

USE/ADVANTAGE - The vaccines are used especially to protect against cholera (both **LPS** and (I) are derived from Vibrio cholerae). They can be admin. intramuscularly or subcutaneously; elicit anti-**LPS** antibodies which are vibriocidal; have very low levels of **endotoxin** (contrast cellular vaccines); can be safely given to children, and can be standardised. When (I) is cholera **toxin**, **toxin**-neutralising antibodies are also produced (and are effective against **toxins** of other species such as E. coli, Campylobacter jejuni or Aeromonas hydrophilia). Antibodies raised against these vaccines can also be used diagnostically, as research reagents and for passive immunisation.

Dwg.0/3

L21 ANSWER 18 OF 29 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1993-093729 [11] WPIDS
DOC. NO. CPI: C1993-041420
TITLE: Escherichia coli O-polysaccharide protein **conjugate** - from isolated O-polysaccharide which is non-toxic and non-pyrogenic.
DERWENT CLASS: B04 D16
INVENTOR(S): CRYZ, S J; FURER, E P
PATENT ASSIGNEE(S): (CRYZ-I) CRYZ S J; (INSS) SWISS SERUM & VACCINE INST
COUNTRY COUNT: 21
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9303765	A1	19930304	(199311)*	EN	32
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL SE					
W: AU CA JP					
AU 9224641	A	19930316	(199328)		
ZA 9206063	A	19930728	(199335)		32
EP 598818	A1	19940601	(199421)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL SE					
US 5370872	A	19941206	(199503)		7
JP 06510530	W	19941124	(199506)		7
EP 598818	A4	19950405	(199613)		
AU 669854	B	19960627	(199636)		
JP 2763960	B2	19980611	(199828)		9
EP 598818	B1	20010131	(200108)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL SE					
DE 69231673	E	20010308	(200121)		
ES 2154263	T3	20010401	(200123)		
CA 2115564	C	20020122	(200216)	EN	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9303765	A1	WO 1992-US6531	19920811
AU 9224641	A	AU 1992-24641	19920811

ZA 9206063	A	ZA 1992-6063	19920812
EP 598818	A1	EP 1992-918016	19920811
		WO 1992-US6531	19920811
US 5370872	A	US 1991-743787	19910812
JP 06510530	W	WO 1992-US6531	19920811
		JP 1993-504334	19920811
EP 598818	A4	EP 1992-918016	
AU 669854	B	AU 1992-24641	19920811
JP 2763960	B2	WO 1992-US6531	19920811
		JP 1993-504334	19920811
EP 598818	B1	EP 1992-918016	19920811
		WO 1992-US6531	19920811
DE 69231673	E	DE 1992-631673	19920811
		EP 1992-918016	19920811
		WO 1992-US6531	19920811
ES 2154263	T3	EP 1992-918016	19920811
CA 2115564	C	CA 1992-2115564	19920811
		WO 1992-US6531	19920811

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9224641	A	Based on	WO 9303765
EP 598818	A1	Based on	WO 9303765
JP 06510530	W	Based on	WO 9303765
AU 669854	B	Previous Publ.	AU 9224641
		Based on	WO 9303765
JP 2763960	B2	Previous Publ.	JP 06510530
		Based on	WO 9303765
EP 598818	B1	Based on	WO 9303765
DE 69231673	E	Based on	EP 598818
		Based on	WO 9303765
ES 2154263	T3	Based on	EP 598818
CA 2115564	C	Based on	WO 9303765

PRIORITY APPLN. INFO: US 1991-743787 19910812

AN 1993-093729 [11] WPIDS

AB WO 9303765 A UPAB: 19931122

Production of an E.coli vaccine comprises (a) purifying **lipopolysaccharide** from E.coli expressing complete O-polysaccharide sidechains; (b) isolating the O-polysaccharide region of the **lipopolysaccharide** molecule by hydrolysis in dilute acetic acid and purifying it essentially free of lipid A; and (c) **covalently** coupling lipid A-free O-polysaccharide via at least one hydroxyl or carboxyl group of said polysaccharide to a carrier protein.

A **conjugate** comprising the O-polysaccharide region of an E.coli **lipopolysaccharide** molecule **covalently** coupled to a carrier protein, is also claimed. It has a mol.weight greater than 600,000, and may further comprises a bifunctional spacer molecule where, the O-polysaccharide is **covalently linked** to said carrier protein through said spacer molecule. The spacer molecule is e.g. **adipic** acid **dihydrazide**. The O-polysaccharide component is pref. exposed to an oxidising agent e.g. NaIO4, for sufficient time to oxidise

40-80% of available reducing sugars.
USE/ADVANTAGE - For production of a polyvalent, non-toxic vaccine against E.coli which is effective against the different E.coli serotypes
Dwg.0/0

ABEQ ZA 9206063 A UPAB: 19931119
The method involves purifying **lipopolysaccharide** from E. coli expressing complete O-polysaccharide sidechains; isolating the O-polysaccharide region of the **lipopolysaccharide** molecule by hydrolysis in dilute acetic acid and purifying it essentially free of lipid A; and **covalently** coupling lipid A-free O-polysaccharide via at least one hydroxyl or carboxyl group of the polysaccharide to a carrier protein.
Polyvalent vaccines are prepared by combining two or more monovalent vaccines for different serotypes prepared according to the present invention. The invention also relates to **conjugates** used in the vaccines. The **conjugates** of the present invention are the O-polysaccharide region of an E. coli **lipopolysaccharide** molecule **covalently** coupled to a carrier protein.

ABEQ US 5370872 A UPAB: 19950126
Prepn. of a polyvalent E. coli vaccine comprises (1) preparing monovalent vaccines from each of the O-polysaccharide serotypes 01, 02, 04, 06, 07, 08, 012, 015, 016, 018, 025 and 075 by (a) purifying **lipopolysaccharide** from E. coli expressing complete O-polysaccharide side chains (b) sepg. the O-polysaccharide region from (a) by dil. acid hydrolysis and purifying free of lipid A; (c) oxidn. reducing sugars of the O-polysaccharide with NaIO4 for 2-5 mins. under conditions to retain antigenicity and produce reactive CHO gps.; (d) sepg. the oxidised O-polysaccharide; (e) then **covalently** coupling it via its OH or COO gp. to a carrier protein; (2) combining the 12 monovalent vaccines of different serotypes resulting from steps (a)-(e) to produce polyvalent vaccine.
Pref. 40-80% of available sugars of the O-polysaccharide are oxidised. Carrier proteins include **toxin** A, which may be coupled via a spacer molecule to the oxidised O-polysaccharide, via its OH or COO gp. **Toxin** A is detoxified by **covalently** coupling with **adipic** acid **dihydrazide**.
ADVANTAGE - The vaccines are effective against all E.coli strains and are non-pyrogenic, nontoxic, immunogenic serotype specific **LPS** based **conjugates**.
Dwg.0/0

L21 ANSWER 19 OF 29 TOXCENTER COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:140952 TOXCENTER
COPYRIGHT: Copyright 2004 ACS
DOCUMENT NUMBER: CA11820198173E
TITLE: Escherichia coli O-polysaccharide-protein **conjugate** vaccine
AUTHOR(S): Cryz, Stanley J.; Furer, Emil P.
PATENT INFORMATION: WO 933765 A1 4 Mar 1993
SOURCE: (1993) PCT Int. Appl., 33 pp.
CODEN: PIXXD2.
COUNTRY: UNITED STATES

DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1993:198173
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020924

AB A polyvalent vaccine composed of nonpyrogenic, nontoxic, immunogenic serotype-specific **lipopolysaccharide** (**LPS**)-based **conjugates**, is prepared by (1) purifying **LPS** from E. coli expressing complete O-polysaccharide side chains, (2) isolating the O-polysaccharide region of the **LPS** mol. by hydrolysis in a dilute AcOH solution and purifying it essentially free of lipid A, and (3) **covalently** coupling lipid A-free O-polysaccharide via at least one OH or CO2H group of the polysaccharide to a carrier protein. Thus, O-polysaccharide was derived from hydrolyzed E. coli **LPS** and **covalently linked** to **toxin** A by using **adipic** acid **dihydrazide** as a spacer mol. The obtained **conjugate** elicited an anti-E. coli **LPS** and an antitoxin A IgG antibody response in both rabbits and humans.

L21 ANSWER 20 OF 29 MEDLINE on STN
ACCESSION NUMBER: 91100002 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1898901
TITLE: Synthesis and characterization of a Pseudomonas aeruginosa alginate-**toxin** A **conjugate** vaccine.
AUTHOR: Cryz S J Jr; Furer E; Que J U
CORPORATE SOURCE: Swiss Serum and Vaccine Institute, Bern, Switzerland.
SOURCE: Infection and immunity, (1991 Jan) 59 (1) 45-50.
Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199102
ENTRY DATE: Entered STN: 19910329
Last Updated on STN: 20020420
Entered Medline: 19910220

AB Alginate from Pseudomonas aeruginosa 3064 was depolymerized by controlled heating in dilute acid. The resulting depolymerized alginate (Mr less than 60,000) was **covalently** coupled to **toxin** A with **adipic** acid **dihydrazide** as a spacer molecule and carbodiimide as a **linker**. The resulting **conjugate** was composed of **toxin** A and depolymerized alginate at a ratio of 4:1 and possessed an Mr of 260,000. The **conjugate** was nontoxic and nonpyrogenic. While native alginate (Mr greater than 640,000) given in a range of doses was poorly immunogenic in mice and rabbits, the **conjugate** induced high levels of antibody which **bound** to native alginate. Rabbits, but not mice, also produced an antitoxin immunoglobulin antibody response. Alginate derived from three other strains of P. aeruginosa competed with the homologous 3064 alginate for **binding** to anticonjugate antibody. This indicates that the **conjugate** elicits an antibody response able to recognize heterologous alginates. The

serum from rabbits immunized with the **conjugate** was effective at promoting the uptake and killing of mucoid strains of P. aeruginosa by human polymorphonuclear leukocytes. In contrast, immunization with native alginate did not engender an opsonic antibody response. Rabbit anticonjugate antibody also neutralized the cytotoxic potential of **toxin** A.

L21 ANSWER 21 OF 29 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 90129288 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2105272
TITLE: Synthesis and characterization of Escherichia coli O18 O-polysaccharide **conjugate** vaccines.
AUTHOR: Cryz S J Jr; Cross A S; Sadoff J C; Furer E
CORPORATE SOURCE: Swiss Serum and Vaccine Institute, Bern, Switzerland.
SOURCE: Infection and immunity, (1990 Feb) 58 (2) 373-7.
Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199002
ENTRY DATE: Entered STN: 19900328
Last Updated on STN: 20020420
Entered Medline: 19900226

AB Nontoxic, serologically reactive O polysaccharide was derived from Escherichia coli O18 **lipopolysaccharide** by acid hydrolysis, extraction with organic solvents, and gel filtration chromatography. Oxidized O polysaccharide was **covalently** coupled to either Pseudomonas aeruginosa **toxin** A or cholera **toxin** by using **adipic** acid **dihydrazide** as a spacer molecule in the presence of carbodiimide. The resulting **conjugates** were composed of approximately equal amounts of O polysaccharide and protein and were nontoxic and nonpyrogenic. Both **conjugates** engendered an immunoglobulin G antibody response in rabbits that recognized native O18 **lipopolysaccharide**. Such antibody was able to promote the uptake and killing of an E. coli O18 strain bearing the K1 capsule by human polymorphonuclear leukocytes. Immunoglobulin G isolated from the sera of rabbits immunized with either **conjugate** afforded protection against an E. coli O18 challenge when passively transferred to mice.

L21 ANSWER 22 OF 29 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 89281144 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2733597
TITLE: Octavalent Pseudomonas aeruginosa O-polysaccharide-**toxin** A **conjugate** vaccine.
AUTHOR: Cryz S J Jr; Sadoff J C; Furer E
CORPORATE SOURCE: Swiss Serum and Vaccine Institute, Berne.
SOURCE: Microbial pathogenesis, (1989 Jan) 6 (1) 75-80.
Journal code: 8606191. ISSN: 0882-4010.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198907

Searcher : Shears 571-272-2528

ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19970203
Entered Medline: 19890725

AB An octavalent Pseudomonas aeruginosa **conjugate** vaccine was synthesized by **covalently** coupling the O-polysaccharide (O-PS) moiety derived from **lipopolysaccharides** of Habs serotypes 1, 2, 3, 4, 5, 6, 11 and 12 to **toxin** A. **Adipic** acid **dihydrazide** was used as a spacer molecule to facilitate **conjugation**. The vaccine was composed of 37% (w/w) O-PS and 63% **toxin** A, devoid of enzymatic activity characteristic of **toxin** A, non-toxic for mice and guinea pigs, and non-pyrogenic. The vaccine elicited a significant rise in immunoglobulin G antibody levels to all serotypes of **lipopolysaccharide** contained in the vaccine and to **toxin** A. Serotypes 6, 10 and 11 were most immunogenic in mice whereas serotypes 1 and 5 engendered the lowest antibody response. Antitoxin A antibody was able to neutralize the cytotoxicity of **toxin** A. Immunization of mice with the vaccine conferred significant protection against subsequent challenge with all P. aeruginosa serotype strains contained in the vaccine.

L21 ANSWER 23 OF 29 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1987-062644 [09] WPIDS
DOC. NO. CPI: C1987-051135
TITLE: Preparation of vaccines against gram-negative bacterial infections - by combining polysaccharide from bacteria **endotoxin** with exo-protein.
DERWENT CLASS: B04 D16
INVENTOR(S): CRYZ, S J; FUERRER, E
PATENT ASSIGNEE(S): (INSS) SCHWEIZ SERUM & IMPFINST; (INSS) SWISS SERUM & VACCINE INST
COUNTRY COUNT: 19
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
PT 83096	A	19870126	(198709)*		33
EP 220387	A	19870506	(198718)	GE	
R: AT BE CH DE FR GB IT LI NL					
JP 62089632	A	19870424	(198722)		
AU 8663229	A	19870402	(198725)		
ZA 8606564	A	19870324	(198726)		
DK 8603207	A	19870328	(198729)		
US 4771127	A	19880913	(198839)		8
ES 2000140	A	19871216	(198911)		
EP 220387	B	19900919	(199038)		
R: AT BE CH DE FR GB IT LI NL SE					
DE 3674328	G	19901025	(199044)		
CA 1276552	C	19901120	(199101)		
JP 06062434	B2	19940817	(199431)		11

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

PT 83096	A	PT 1986-83096	19860729
EP 220387	A	EP 1986-110114	19860723
JP 62089632	A	JP 1986-180233	19860801
ZA 8606564	A	ZA 1986-6564	19860829
US 4771127	A	US 1986-892846	19860804
JP 06062434	B2	JP 1986-180233	19860801

FILING DETAILS:

PATENT NO	KIND	PATENT NO
JP 06062434	B2 Based on	JP 62089632

PRIORITY APPLN. INFO: CH 1985-4199 19850927

AN 1987-062644 [09] WPIDS

AB PT 83096 A UPAB: 19930922

Non-toxic **conjugated** vaccines against gram-negative bacterial infections comprise a type-specific polysaccharide and a protein which are **covalently bound** together. The polysaccharide is derived from the bacterial **endotoxin** and the protein is an exoprotein (claimed). The **conjugated** vaccine is especially used against Pseudomonas aeruginosa and E.coli The exoprotein is pref. a exotoxin or exotoxoid and the exotoxin is pref. **toxin** A from P aeruginosa The exotoxoid is pref. tetranustoxoid or diptheriatoxoid. The vaccine pref. consists of a mixture of 3-15 **conjugates**, the polysaccharide being obtd. from 3-15 various types of the same type of bacteria.

Polyvalent vaccines comprise mixts of **conjugated** vaccines, the individual components producing antibodies against specific bacteria types. The **conjugate** vaccines are used in the production of hyperimmunosera, which in turn serve-as immunoglobulins which are delivered intravenous or intramuscularly.

USE/ADVANTAGE - For use especially in hospitals with patients being treated with immunosuppressives to prevent secondary infections. (First major country equivalent to PT-83096-A)

0/0

ABEQ EP 220387 B UPAB: 19930922

Non-toxic **conjugated** vaccines against gram-negative bacterial infections comprise a type-specific polysaccharide and a protein which are **covalently bound** together. The polysaccharide is derived from the bacterial **endotoxin** and the protein is an exoprotein (claimed). The **conjugated** vaccine is esp. used against Pseudomonas aeruginosa and E.coli The exoprotein is pref. a exotoxin or exotoxoid and the exotoxin is pref. **toxin** A from P aeruginosa The exotoxoid is pref. tetranustoxoid or diptheriatoxoid. The vaccine pref. consists of a mixt. of 3-15 **conjugates**, the polysaccharide being obtd. from 3-15 various types of the same type of bacteria.

Polyvalent vaccines comprise mixts of **conjugated** vaccines, the individual components producing antibodies against specific bacteria types. The **conjugate** vaccines are used in the prodn. of hyperimmunosera, which in turn serve-as immunoglobulins which are delivered intravenous or intramuscularly.

USE/ADVANTAGE - For use esp. in hospitals with patients being treated with immunosuppressives to prevent secondary infections. (First major country equivalent to PT-83096-A)

0/0
ABEQ US 4771127 A UPAB: 19930922
Immunogenic **conjugate** comprises a Pseudomonas aeruginosa polysaccharide which is free from lipid-A, **covalently linked** through one or more OH and/or COOH gps. to a tetanus **toxoid** carrier protein or **toxin**-A carrier protein.
Pref. **linking** agent is **adipic dihydrazide**.
USE - The prods. are nontoxic and not pyrogenic and are immunising agents for protection against tetanus **toxin** or **toxin**-A.

L21 ANSWER 24 OF 29 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 86306057 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3091708
TITLE: Pseudomonas aeruginosa polysaccharide-tetanus **toxoid conjugate** vaccine: safety and immunogenicity in humans.
AUTHOR: Cryz S J Jr; Sadoff J C; Furer E; Germanier R
SOURCE: Journal of infectious diseases, (1986 Oct) 154 (4) 682-8.
Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198610
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19970203
Entered Medline: 19861023

AB A Pseudomonas aeruginosa polysaccharide-tetanus **toxoid** (Ttxd) **conjugate** vaccine was produced. Polysaccharide was derived from **lipopolysaccharide** (**LPS**) and **covalently linked** to Ttxd by using carbodiimide with **adipic** acid **dihydrazide** as a spacer molecule. The **conjugate** possessed a relative molecular weight of greater than 350,000 and was nontoxic and nonpyrogenic. The vaccine **bound** serospecific monoclonal antibodies with an avidity similar to **LPS** and reacted with murine and human opsonic antibody. The vaccine was immunogenic in rabbits and mice and elicited IgG antibody to both **LPS** and Ttxd. The vaccine was safe when parenterally administered to humans and evoked only mild, transient reactions. Mean titers of IgG antibody to **LPS** rose 19-fold after immunization, with 82% of the volunteers responding with a fourfold or greater rise in titer. IgG antibody to **LPS** evoked after immunization was opsonic and highly effective at preventing fatal experimental burn wound sepsis due to P. aeruginosa.

L21 ANSWER 25 OF 29 EMBASE on STN
ACCESSION NUMBER: 86246479 EMBASE
DOCUMENT NUMBER: 1986246479
TITLE: Pseudomonas aeruginosa polysaccharide-tetanus **toxoid conjugate** vaccine: Safety and immunogenicity in humans.

AUTHOR: Cryz Jr. S.J.; Sadoff J.C.; Furer E.; Germanier R.
CORPORATE SOURCE: Swiss Serum and Vaccine Institute, P.O. Box 2707, CH-3001 Bern, Switzerland
SOURCE: Journal of Infectious Diseases, (1986) 154/4 (682-688).
CODEN: JIDIAQ
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English

AB A Pseudomonas aeruginosa polysaccharide-tetanus **toxoid** (Ttxd) **conjugate** vaccine was produced. Polysaccharide was derived from **lipopolysaccharide** (**LPS**) and **covalently linked** to Ttxd by using carbodiimide with **adipic** acid **dihydrazide** as a spacer molecule. The **conjugate** possessed a relative molecular weight of >350,000 and was nontoxic and nonpyrogenic. The vaccine **bound** serospecific monoclonal antibodies with an avidity similar to **LPS** and reacted with murine and human opsonic antibody. The vaccine was immunogenic in rabbits and mice and elicited IgG antibody to both **LPS** and Ttxd. The vaccine was safe when parenterally administered to humans and evoked only mild, transient reactions. Mean titers of IgG antibody to **LPS** rose 19-fold after immunization, with 82% of the volunteers responding with a fourfold or greater rise in titer. IgG antibody to **LPS** evoked after immunization was opsonic and highly effective at preventing fatal experimental burn wound sepsis due to P. aeruginosa.

L21 ANSWER 26 OF 29 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 86166807 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3082756
TITLE: Pseudomonas aeruginosa immunotype 5 polysaccharide-**toxin** A **conjugate** vaccine.
AUTHOR: Cryz S J Jr; Furer E; Sadoff J C; Germanier R
SOURCE: Infection and immunity, (1986 Apr) 52 (1) 161-5.
Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198605
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19860501

AB Polysaccharide (PS) derived from Pseudomonas aeruginosa immunotype 5 **lipopolysaccharide** was **covalently** coupled to **toxin** A by reductive amination with **adipic** acid **dihydrazide** as a spacer molecule. The resulting PS-**toxin** A **conjugate** was composed of 27.5% PS and 72.5% **toxin** A. The **conjugate** was composed of heterogeneous high-molecular-weight species, all of which possessed an Mr greater than 670,000. The **conjugate** was nontoxic for mice and nonpyrogenic at a dose of 50 micrograms/kg of body

weight when intravenously administered to rabbits. Immunization of rabbits with the **conjugate** evoked both an antilipopolysaccharide immunoglobulin G (IgG) and an anti-**toxin** A IgG response. Anticonjugate IgG was capable of neutralizing the cytotoxic effect of **toxin** A. Immunization of mice with the **conjugate** increased the mean lethal dose from 4.5 X 10(1) P. aeruginosa for control mice to 9.6 X 10(5) P. aeruginosa for vaccinated mice. Similarly, immunization raised the mean lethal dose for **toxin** A from 0.2 to 4.67 micrograms per mouse.

L21 ANSWER 27 OF 29 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 86126756 EMBASE
DOCUMENT NUMBER: 1986126756
TITLE: Pseudomonas aeruginosa immunotype 5 polysaccharide-**toxin** A **conjugate** vaccine.
AUTHOR: Cryz Jr. S.J.; Furer E.; Sadoff J.C.; Germanier R.
CORPORATE SOURCE: Swiss Serum and Vaccine Institute, 3001 Berne, Switzerland
SOURCE: Infection and Immunity, (1986) 52/1 (161-165). CODEN: INFIBR
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
LANGUAGE: English

AB Polysaccharide (PS) derived from Pseudomonas aeruginosa immunotype 5 **lipopolysaccharide** was **covalently** coupled to **toxin** A by reductive amination with **adipic** acid **dihydrazide** as a spacer molecule. The resulting PS-**toxin** A **conjugate** was composed of 27.5% PS and 72.5% **toxin** A. The **conjugate** was composed of heterogeneous high-molecular-weight species, all of which possessed an M(r) >670,000. The **conjugate** was nontoxic for mice and nonpyrogenic at a dose of 50 μg/kg of body weight when intravenously administered to rabbits. Immunization of rabbits with the **conjugate** evoked both an antilipopolysaccharide immunoglobulin G (IgG) and an anti-**toxin** A IgG response. Anticonjugate IgG was capable of neutralizing the cytotoxic effect of **toxin** A. Immunization of mice with the **conjugate** increased the mean lethal dose from 4.5 x 101 P. aeruginosa for control mice to 9.6 x 105 P. aeruginosa for vaccinated mice. Similarly, immunization raised the mean lethal dose for **toxin** A from 0.2 to 4.67 μg per mouse.

L21 ANSWER 28 OF 29 TOXCENTER COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1981:120806 TOXCENTER
COPYRIGHT: Copyright 2004 ACS
DOCUMENT NUMBER: CA09513113154H
TITLE: Preparation and characterization of detoxified **lipopolysaccharide**-protein **conjugates**
AUTHOR(S): Seid, Robert C., Jr.; Sadoff, Jerald C.
CORPORATE SOURCE: Walter Reed Army Med. Cent., Walter Reed Army Inst. Res., Washington, DC, 20012, USA.

SOURCE: Journal of Biological Chemistry, (1981) Vol. 256, No. 14, pp. 7305-10.
CODEN: JBCHA3. ISSN: 0021-9258.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1981:513154
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20021203

AB Alkaline treatment of Pseudomonas aeruginosa type 5 **lipopolysaccharide** (**LPS**) resulted in reduced toxicity as measured by both the Limulus amoebocyte assay and the rabbit pyrogenicity test. Chemical anal. of the deacylated **LPS** (D-**LPS**) revealed that ester-**linked** fatty acids were removed whereas the amide-**linked** fatty acids remained intact. The neutral and amino sugar compns. for native **LPS** and D-**LPS** were identical within exptl. error. Antigenic determinants for complement-dependent human opsonic antibody were retained under these deacylation conditions. To enhance its immunogenicity, D-**LPS** was **covalently** coupled to Pseudomonas **pili** and the 1,4-diaminobutyl derivs. of Pseudomonas exotoxin A and tetanus **toxoid**. Quant. amino sugar analyses revealed that 2.6 and 3.2 mol of D-**LPS** were **covalently bound** to aminobutyl Pseudomonas exotoxin A and aminobutyl tetanus **toxoid**, resp. Gel electrophoresis data indicated ≥1 mol of D- **LPS** **covalently bound**/pilus subunit protein. Initial immunol. data indicated that antibody against D-**LPS** could be induced when the D-**LPS** is **covalently** attached to protein carriers.

L21 ANSWER 29 OF 29 TOXCENTER COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:531305 TOXCENTER
DOCUMENT NUMBER: CRISP-94-D01303-10
TITLE: **CONJUGATE** INDUCED POLYSACCHARIDE ANTIBODIES
AUTHOR(S): SZU S C
CORPORATE SOURCE: NICHD, NIH
SUPPORTING ORGANIZATION (SPONSORING AGENCY): U.S. DEPT. OF HEALTH AND HUMAN SERVICES; PUBLIC HEALTH SERVICE; NATIONAL INST. OF HEALTH, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
SOURCE: Crisp Data Base National Institutes Of Health.
DOCUMENT TYPE: (Research)
FILE SEGMENT: CRISP
LANGUAGE: English
ENTRY DATE: Entered STN: 20021200
Last Updated on STN: 20021200

AB Polysaccharides, from capsule or from the **LPS** of Gram-negative enteric pathogens, are **covalently** **conjugated** to carrier proteins to increase their immunogenicity. Conditions for optimal derivatization of the saccharides, proteins and **conjugation** of the two are investigated. A new approach to synthesize Vi **conjugate** without disulfide **linkages** was devised. The carboxylic

groups on Vi polysaccharide was derivatized with **adipic dihydrazide** through carbodiimide. The derivatized Vi could then **bind** to proteins through carbodiimide. The **LPS** of Vibro cholerae is a virulence factor and potential protective antigen. The toxicity of the **LPS** was greatly reduced by treatment in an organic base. The treatment retained most of the **LPS** structure. **Conjugates** made with the detoxified **LPS** and cholera **toxin** induced vibrocidal antibodies in laboratory animals. Similar techniques were devised for preparing polysaccharide of Salmonella typhimurium, E. coli 0111 for diarrhea diseases, mutant J5 for **endotoxin** shock and 0157 for gastroenteritis.

(FILE 'MEDLINE' ENTERED AT 15:00:16 ON 03 JUN 2004)

L22	33569	SEA FILE=MEDLINE ABB=ON	PLU=ON	LIPOPOLYSACCHARIDES/CT
L23	49171	SEA FILE=MEDLINE ABB=ON	PLU=ON	ANTIGENS/CT
L24	517	SEA FILE=MEDLINE ABB=ON	PLU=ON	L22 AND L23
L25	67732	SEA FILE=MEDLINE ABB=ON	PLU=ON	"CARRIER PROTEINS"/CT
L26	5	SEA FILE=MEDLINE ABB=ON	PLU=ON	L24 AND L25

L22	33569	SEA FILE=MEDLINE ABB=ON	PLU=ON	LIPOPOLYSACCHARIDES/CT
L25	67732	SEA FILE=MEDLINE ABB=ON	PLU=ON	"CARRIER PROTEINS"/CT
L27	688	SEA FILE=MEDLINE ABB=ON	PLU=ON	L22 AND L25
L28	6266	SEA FILE=MEDLINE ABB=ON	PLU=ON	"NEISSERIA GONORRHOEAE"/CT
L29	4	SEA FILE=MEDLINE ABB=ON	PLU=ON	L27 AND L28

L30 9 L26 OR L29

L30 ANSWER 1 OF 9 MEDLINE on STN

ACCESSION NUMBER: 2002632283 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12390351
TITLE: The role of lipooligosaccharide in Neisseria gonorrhoeae pathogenesis of cervical epithelia: lipid A serves as a C3 acceptor molecule.
AUTHOR: Edwards Jennifer L; Apicella Michael A
CORPORATE SOURCE: Department of Microbiology, The University of Iowa, BSB 3-403, 51 Newton Road, Iowa City, IA 52242, USA.
CONTRACT NUMBER: 5T32 HL 07638 (NHLBI)
AI 38515 (NIAID)
AI 45728 (NIAID)
AI43924 (NIAID)
SOURCE: Cellular microbiology, (2002 Sep) 4 (9) 585-98.
Journal code: 100883691. ISSN: 1462-5814.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200211
ENTRY DATE: Entered STN: 20021023
Last Updated on STN: 20021213
Entered Medline: 20021121
ED Entered STN: 20021023
Last Updated on STN: 20021213
Entered Medline: 20021121

AB The use of primary, human, ecto- and endocervical epithelial cell cultures has increased our understanding of the pathogenesis of gonococcal infection in women. Primary cervical epithelial cells express complement (C') receptor type 3 (CR3) and C' proteins required for alternative pathway (AP) activity. Gonococcus -induced membrane ruffling and cellular invasion of primary cervical epithelia is mediated by CR3 and requires co-operative CR3 binding by gonococcus-bound iC3b, porin and pilus. We have extended these studies to identify the site of C3 deposition upon gonococci within the cervical microenvironment. By immunoprecipitation and ELISA we demonstrate that covalent and non-covalent associations occurred between gonococcal LOS and C' protein C3. Sialylation or LOS truncation did not alter the gonococcus-CR3 interaction. By Western blot analysis we observed comparable C3 opsonization patterns among a panel of LOS truncation mutants, sialylated wild-type gonococci, or wild-type bacteria that were not sialylated. Quantitative association/invasion assays performed in the presence or absence of LOS competimers support C3b deposition on the lipid A core structure. Our findings demonstrate a role for lipid A as a C3 acceptor site and suggest that multiple factors govern C3b deposition and its subsequent conversion to iC3b on the surface of the gonococcus within the cervical microenvironment.

L30 ANSWER 2 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2002215477 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11937567
TITLE: Regulation of the mannan-binding lectin pathway of complement on Neisseria gonorrhoeae by C1-inhibitor and alpha 2-macroglobulin.
AUTHOR: Gulati Sunita; Sastry Kedarnath; Jensenius Jens C; Rice Peter A; Ram Sanjay
CORPORATE SOURCE: Section of Infectious Diseases and Hematology-Oncology, Evans Biomedical Research Center, Boston University Medical Center, Boston, MA 02118, USA.. sgulati@bu.edu
CONTRACT NUMBER: AI32725 (NIAID)
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2002 Apr 15) 168 (8) 4078-86.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020416
Last Updated on STN: 20020528
Entered Medline: 20020523

ED Entered STN: 20020416
Last Updated on STN: 20020528
Entered Medline: 20020523

AB We examined complement activation by Neisseria gonorrhoeae via the mannan-binding lectin (MBL) pathway in normal human serum. Maximal binding of MBL complexed with MBL-associated serine proteases (MASPs) to N. gonorrhoeae was achieved at a concentration of 0.3 microg/ml. Preopsonization with MBL-MASP at concentrations as low as 0.03 microg/ml resulted in approximately 60% killing of otherwise

fully serum-resistant gonococci. However, MBL-depleted serum (MBLdS) reconstituted with MBL-MASP before incubation with organisms (postopsonization) failed to kill at a 100-fold higher concentration. Preopsonized organisms showed a 1.5-fold increase in C4, a 2.5-fold increase in C3b, and an approximately 25-fold increase in factor Bb binding; enhanced C3b and factor Bb binding was classical pathway dependent. Preopsonization of bacteria with a mixture of pure C1-inhibitor and/or alpha(2)-macroglobulin added together with MBL-MASP, all at physiologic concentrations before adding MBLdS, totally reversed killing in 10% reconstituted serum. Reconstitution of MBLdS with supraphysiologic (24 microg/ml) concentrations of MBL-MASP partially overcame the effects of inhibitors (57% killing in 10% reconstituted serum). We also examined the effect of sialylation of gonococcal lipooligosaccharide (LOS) on MBL function. Partial sialylation of LOS did not decrease MBL or C4 binding but did decrease C3b binding by 50% and resulted in 80% survival in 10% serum (lacking bacteria-specific Abs) even when sialylated organisms were preopsonized with MBL. Full sialylation of LOS abolished MBL, C4, and C3b binding, resulting in 100% survival. Our studies indicate that MBL does not participate in complement activation on N. gonorrhoeae in the presence of "complete" serum that contains C1-inhibitor and alpha(2)-macroglobulin.

L30 ANSWER 3 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2000316011 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10858200
TITLE: The lipopolysaccharide structures of Salmonella enterica serovar Typhimurium and Neisseria gonorrhoeae determine the attachment of human mannose-binding lectin to intact organisms.
AUTHOR: Devyatyarova-Johnson M; Rees I H; Robertson B D; Turner M W; Klein N J; Jack D L
CORPORATE SOURCE: Immunobiology Unit, Institute of Child Health, London WC1N 1EH, United Kingdom.
SOURCE: Infection and immunity, (2000 Jul) 68 (7) 3894-9. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000728
Last Updated on STN: 20000728
Entered Medline: 20000720

ED Entered STN: 20000728
Last Updated on STN: 20000728
Entered Medline: 20000720

AB Mannose-binding lectin (MBL) is an important component of the innate immune system. It binds to the arrays of sugars commonly presented by microorganisms and activates the complement system independently of antibody. Despite detailed knowledge of the stereochemical basis of MBL binding, relatively little is known about how bacterial surface structures influence binding of the lectin. Using flow cytometry, we have measured the binding of MBL to a range of mutants of Salmonella enterica serovar Typhimurium and Neisseria gonorrhoeae

which differ in the structure of expressed lipopolysaccharide (LPS). For both organisms, the possession of core LPS structures led to avid binding of MBL, which was abrogated by the addition of O antigen (Salmonella serovar Typhimurium) or sialic acid (N. gonorrhoeae). Truncation of the LPS within the core led to lower levels of MBL binding. It was not possible to predict the magnitude of MBL binding from the identity of the LPS terminal sugar alone, indicating that the three-dimensional disposition of LPS molecules is probably also of importance in determining MBL attachment. These results further support the hypothesis that LPS structure is a major determinant of MBL binding.

L30 ANSWER 4 OF 9 MEDLINE on STN
ACCESSION NUMBER: 97162299 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9009286
TITLE: Nramp1 transfection transfers Ity/Lsh/Bcg-related pleiotropic effects on macrophage activation: influence on antigen processing and presentation.
AUTHOR: Lang T; Prina E; Sibthorpe D; Blackwell J M
CORPORATE SOURCE: Unite d'Immunophysiologie Cellulaire, Institut Pasteur, Paris, France.
SOURCE: Infection and immunity, (1997 Feb) 65 (2) 380-6. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970306
Last Updated on STN: 19970306
Entered Medline: 19970221

ED Entered STN: 19970306
Last Updated on STN: 19970306
Entered Medline: 19970221

AB The natural resistance-associated macrophage protein (Nramp1) regulates macrophage activation. One of its pleiotropic effects on macrophage function is to regulate expression of major histocompatibility class II molecules. In this study macrophages stably transfected with the wild-type (infection-resistant) or the natural mutant (infection-susceptible) allele of the Nramp1 gene were used to study class II expression and processing and presentation of recombinant protein antigens to CD4+ T-cell hybridomas. As demonstrated previously for macrophages from Nramp1-resistant and -susceptible congenic mouse strains, transfected macrophage clones carrying the wild-type allele showed enhanced upregulation of class II molecules in response to gamma interferon compared to that shown by macrophage clones carrying an endogenous mutant allele or transfected with the mutant allele expressed under a viral long terminal repeat promoter. The wild-type allele-transfected macrophage clones also demonstrated an enhanced, lipopolysaccharide-dependent ability to process the recombinant leishmanial antigen LACK-delta 1 (the Leishmania homolog of receptors for activated C kinase) for presentation to LACK-specific CD4+ T cells. An influence on antigen processing must therefore be added to the growing list of pleiotropic effects of the Nramp1 gene potentially contributing to its role in infectious and

autoimmune disease susceptibility. These results also have important implications for analysis of T-cell responses to vaccination, especially where antigens are presented to the immune system using live Salmonella species or Mycobacterium bovis BCG as a vaccine vehicle.

L30 ANSWER 5 OF 9 MEDLINE on STN
ACCESSION NUMBER: 95043546 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7955527
TITLE: Heat shock proteins as carrier molecules: in vivo helper effect mediated by Escherichia coli GroEL and DnaK proteins requires cross-linking with antigen.
COMMENT: Comment in: Clin Exp Immunol. 1994 Nov;98(2):175-7. PubMed ID: 7955518
AUTHOR: Barrios C; Georgopoulos C; Lambert P H; Del Giudice G
CORPORATE SOURCE: Department of Pathology, University of Geneva, Centre Medical Universitaire, Switzerland.
SOURCE: Clinical and experimental immunology, (1994 Nov) 98 (2) 229-33.
Journal code: 0057202. ISSN: 0009-9104.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 19950110
Last Updated on STN: 19950110
Entered Medline: 19941212

ED Entered STN: 19950110
Last Updated on STN: 19950110
Entered Medline: 19941212

AB In the past few years we have shown that mycobacterial heat shock proteins (hsp) of 65 and 70 kD exert a very strong helper effect in mice and monkeys when conjugated to peptides and oligosaccharides and given in the absence of adjuvants. In the present study we show that this adjuvant-free helper effect (i) is not due to lipopolysaccharide (LPS), since it was observed in LPS-resistant mice (C3H/HeJ) immunized with hsp-based constructs containing the malaria peptide (NANP)40, and (ii) is characteristic of hsp, since it was not observed with conjugates containing the mycobacterial p38 antigen, which is not a stress protein. Interestingly, the hsp GroEL and DnaK of Escherichia coli, which share a high degree of homology with the mycobacterial 65-kD and 70-kD hsp, respectively, exhibit a strong in vivo helper effect when conjugated to the (NANP)40 peptide, and the conjugates given in the absence of adjuvants. This in vivo helper behaviour of the GroEL and DnaK proteins corresponds well to that observed with the mycobacterial 65-kD and 70-kD hsp, respectively, since the hsp65- and GroEL-based constructs require previous priming of the animals with live bacille Calmette-Guerin (BCG), which is not needed for the hsp70- and DnaK-based constructs. Finally, using both mycobacterial and E. coli hsp we show that their in vivo helper effect in the absence of adjuvants requires cross-linking to the synthetic peptide. Taken together, our results suggest that the adjuvant-free helper effect observed with mycobacterial and E. coli hsp may be a generalized phenomenon, exhibited by hsp from diverse microorganisms. These

findings may find applications in the design of vaccine constructs.

L30 ANSWER 6 OF 9 MEDLINE on STN
ACCESSION NUMBER: 94151707 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8108753
TITLE: Characterization of multiresistant strains of Neisseria gonorrhoeae isolated in Nicaragua.
AUTHOR: Castro I; Bergeron M G; Chamberland S
CORPORATE SOURCE: Departement de Microbiologie, Faculte de Medecine, Universite Laval, Quebec, Canada.
SOURCE: Sexually transmitted diseases, (1993 Nov-Dec) 20 (6) 314-20.
Journal code: 7705941. ISSN: 0148-5717.
Report No.: PIP-091754; POP-00228516.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Population
ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 19940330
Last Updated on STN: 20021101
Entered Medline: 19940324

ED Entered STN: 19940330
Last Updated on STN: 20021101
Entered Medline: 19940324

AB The extensive use of antibiotics in Nicaragua raises concerns about the resulting levels of susceptibility of pathogenic bacteria. This is the first study that characterizes 18 strains of N. gonorrhoeae isolated in Nicaragua (1989), for their antibiotic susceptibility. Strains were predominantly of the auxotype/serotype Proto/PIB. There was no difference in lipopolysaccharides profiles obtained after SDS-PAGE for all strains. Variable expression of the PII outer membrane protein was not associated to antimicrobial resistance. All strains were susceptible to ceftriaxone, spectinomycin, rifampin and cefoxitin. The strains were classified in five groups based on plasmid profiles. A total of 78% of the isolates were penicillinase-producing (PPNG) and 22% were tetracycline-resistant N. gonorrhoeae (TRNG). One PPNG strain showed a concomitant decreased of penicillin binding to penicillin-binding protein 2. These randomly chosen isolates of N. gonorrhoeae from Nicaragua possess high levels of resistance to multiple families of drugs. In Nicaragua, in 1989, health workers obtained urethral or cervical samples from 18 people with gonorrhea attending public health clinics in Managua and sent them to the National Laboratory of Public Health in Managua for characterization of their antibiotic susceptibility. Of the 18 strains, 15 (83.3%) were of the auxotype/serotype Proto/PIB. Electrophoresis of lipopolysaccharides on SDS-polyacrylamide gels (15%) with 4 M urea revealed no difference in lipopolysaccharide profiles for all strains. The variable expression of the 31-kDa opacity outer membrane protein was not related to antimicrobial resistance. All isolates exhibited susceptibility to ceftriaxone, spectinomycin, cefazolin, cefoxitin, and rifampin. 78% of the strains produced beta-lactamase. 89% of the strains were resistant to penicillin and ampicillin, 44% were resistant to tetracycline, 28% were resistant to cefamandol, 22% were resistant to chloramphenicol, and 11% were

resistant to erythromycin. There were 5 distinct groups of Neisseria gonorrhoeae isolated according to their plasmid profiles. The largest was plasmid profile group 1 (55.6%), defined as carrying the 24.5, 3.2, and 2.6 MDa plasmids. It produced beta-lactamase. Penicillinase-producing N. gonorrhoeae (PPNG) comprised 78% of the isolates, 22% of whom were tetracycline-resistant N. gonorrhoea. One PPNG strain exhibited a parallel decrease of penicillin binding to penicillin-binding protein 2. These findings confirmed the presence of multiresistant N. gonorrhoeae strains in Managua, Nicaragua. Based on these findings, the researchers recommended that penicillin and tetracycline not be used to treat gonorrhea in Nicaragua; they recommended ceftriaxone and spectinomycin.

L30 ANSWER 7 OF 9 MEDLINE on STN
ACCESSION NUMBER: 79068998 MEDLINE
DOCUMENT NUMBER: PubMed ID: 82602
TITLE: Mechanisms of clonal abortion tolerogenesis. I. Response of immature hapten-specific B lymphocytes.
AUTHOR: Nossal G J; Pike B L
SOURCE: Journal of experimental medicine, (1978 Nov 1) 148 (5) 1161-70.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197902
ENTRY DATE: Entered STN: 19900314
Last Updated on STN: 19970203
Entered Medline: 19790223
ED Entered STN: 19900314
Last Updated on STN: 19970203
Entered Medline: 19790223

L30 ANSWER 8 OF 9 MEDLINE on STN
ACCESSION NUMBER: 76025980 MEDLINE
DOCUMENT NUMBER: PubMed ID: 51890
TITLE: T lymphocyte-enriched murine peritoneal exudate cells. I. A reliable assay for antigen-induced T lymphocyte proliferation.
AUTHOR: Schwartz R H; Jackson L; Paul W E
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (1975 Nov) 115 (5) 1330-8.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197512
ENTRY DATE: Entered STN: 19900313
Last Updated on STN: 19900313
Entered Medline: 19751230
ED Entered STN: 19900313
Last Updated on STN: 19900313
Entered Medline: 19751230
AB The in vitro activation of murine thymus-derived (T) lymphocytes by

soluble protein and synthetic antigens has been difficult to assess because of the lack of a specific and reliable proliferation assay. The present report describes the development of an assay system which overcomes these problems by making use of a population of nylon wool column-purified T lymphocytes obtained from thioglycollate-induced peritoneal exudates of immunized mice. PETLES (peritoneal exudate, T lymphocyte-enriched cells) were composed mainly of T lymphocytes, eosinophils and small numbers of macrophages. Contamination with bone marrow-derived (B) lymphocytes averaged only 2%. When PETLES from immunized mice were stimulated in microtiter cultures with the immunizing antigen, large degrees of proliferation ensued as measured by incorporation of 3H-methyl-thymidine 5 days after initiation. As few as 1.25 x 10(4) cells and as little as 50 ng/ml of antigen gave significant stimulation. Maximum responses were obtained witn a series of 10 experiments under these optimal conditions, gave a mean incorporation of 70,900 cpm while the controls cultured without antigen showed only 3,600 cpm. PETLES from nonimmunized mice or from mice immunized to other antigens did not respond to DNP5OVA although they did respond to mitogens. The antigen-induced proliferation was shown to require the presence of immune T lymphocytes by two criteria: elimination of the response by treatment with anti-Thy 1.2 serum plus complement and failure to reconstitute the response when the few remaining immune B lymphocytes left after anti-Thy 1.2 treatment were added to nonimmune T lymphocytes. In addition, the system exhibited carrier specificity. Because of the paucity of B lymphocytes in the population, their contribution to the overall magnitude of the proliferative response was negligible as demonstrated by the small response to B cell mitogens. Thus, the assay appears to be a quantitative as well as a qualitative assay for one aspect of T lymphocyte function. This technique should prove useful for the study of murine T lymphocytes in vitro.

L30 ANSWER 9 OF 9 MEDLINE on STN
ACCESSION NUMBER: 75059434 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4140153
TITLE: Cells involved in the in vitro stimulation by DNP-carrier complexes of in vivo primed mouse spleen cells.
AUTHOR: Snippe H; van Eyk R V
SOURCE: Immunology, (1974 Nov) 27 (5) 771-9.
Journal code: 0374672. ISSN: 0019-2805.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197503
ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 19900310
Entered Medline: 19750310
ED Entered STN: 19900310
Last Updated on STN: 19900310
Entered Medline: 19750310

FILE 'HCAPLUS' ENTERED AT 15:45:12 ON 03 JUN 2004

Searcher : Shears 571-272-2528

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L43           3 SEA ABB=ON  PLU=ON  L16 AND (ADIPOYLDIHYDRAZIDE OR (ET
                OR ETHYL)(S)?CARBODIIMIDE OR ETHYLCARBODIIMIDE)
L44           0 SEA ABB=ON  PLU=ON  L43 NOT L19

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC,
     PHIN, TOXCENTER, PASCAL, DISSABS, FEDRIP' ENTERED AT 15:46:02 ON 03
     JUN 2004
L45          11 SEA ABB=ON  PLU=ON  L43
L46           0 SEA ABB=ON  PLU=ON  L45 NOT L20
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(FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER, PASCAL, DISSABS, FEDRIP' ENTERED AT 15:12:11 ON 03 JUN 2004)

- Author (S)

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L31          141 S ("ATUMUGHAM R"? OR "ARUMUGHAM R"?)/AU
L32          301 S ("FORTUNA NEVIN M"? OR "NEVIN FORTUNA M"? OR "NEVIN M"?
                   OR "FORTUNA M"?)/AU
L33         1078 S "APICELLA M"?/AU
L34         2501 S "GIBSON B"?/AU

L35            7 SEA ABB=ON  PLU=ON  L31 AND L32 AND L33 AND L34
L36           10 SEA ABB=ON  PLU=ON  L31 AND (L32 OR L33 OR L34)
L37            7 SEA ABB=ON  PLU=ON  L32 AND (L33 OR L34)
L38          173 SEA ABB=ON  PLU=ON  L33 AND L34
L39           69 SEA ABB=ON  PLU=ON  (L38 OR L31 OR L32 OR L33 OR L34)
                 AND L14
L40           47 SEA ABB=ON  PLU=ON  L39 AND (LINK? OR CONJUGAT? OR BOND
                 OR BONDED OR BOUND OR BIND? OR CROSSLINK?)
L41           52 SEA ABB=ON  PLU=ON  L35 OR L36 OR L37 OR L40
L42           20 DUP REM L41 (32 DUPLICATES REMOVED)
```

L42 ANSWER 1 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2003:887632 HCAPLUS
DOCUMENT NUMBER: 139:363588
TITLE: Antigenic **conjugates** of conserved **lipopolysaccharides** of Gram-negative bacteria
INVENTOR(S): **Arumugham, Rasappa G.; Fortuna-Nevin, Maria; Apicella, Michael A.; Gibson, Bradford W.**
PATENT ASSIGNEE(S): Wyeth Holdings Corporation, USA
SOURCE: U.S., 13 pp., Cont.-in-part of U.S. Provisional Ser. No. 88,364.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6645503	B1	20031111	US 1999-264747	19990309
US 2004052804	A1	20040318	US 2003-643314	20030819

PRIORITY APPLN. INFO.: US 1998-88364P P 19980310
US 1999-264747 A3 19990309

AB The authors disclose **conjugates** comprising a carrier protein covalently **bonded** to the conserved portion of a **lipopolysaccharide** of a Gram-neg. bacterium. The conserved portion of the **lipopolysaccharide** comprises the inner core and lipid A portions of the **lipopolysaccharide**. The **conjugate** elicits a cross-reactive immune response against heterologous strains of the Gram neg. bacterium.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 2 OF 20 DISSABS COPYRIGHT (C) 2004 ProQuest Information and

ACCESSION NUMBER: 2003:3848 DISSABS Order Number: AAI3050793
TITLE: Complement opsonization and direct adherence of Neisseria gonorrhoeae to complement receptor type 3 mediate cervical cell invasion
AUTHOR: Edwards, Jennifer Lynn [Ph.D.]; **Apicella, Michael A. [adviser]**
CORPORATE SOURCE: The University of Iowa (0096)
SOURCE: Dissertation Abstracts International, (2002) Vol. 63, No. 4B, p. 1679. Order No.: AAI3050793. 344 pages. ISBN: 0-493-65364-3.
DOCUMENT TYPE: Dissertation
FILE SEGMENT: DAI
LANGUAGE: English

AB The clinical manifestations of Neisseria gonorrhoeae infection suggest that pathogenesis differs between men and women. To study gonococcal pathogenesis in a model system that would be reflective of the lower female genital tract we developed primary, human, ecto- and endocervical cell systems. Our studies demonstrate that complement receptor type 3 (CR3) is present on cervical, but not male urethral, epithelia. CR3-mediated endocytosis serves as a primary mechanism by which the gonococcus is able to elicit membrane ruffling and macropinocytosis of the cervical epithelium. Examination of clinical biopsies derived from women with culture documented gonococcal cervicitis confirmed these findings.

Primary cervical epithelial cells produce alternative pathway (AP) complement (C') components. Deposition of C' protein C3 upon the gonococcus surface and its rapid inactivation to iC3b mediate adherence to the I-domain of CR3. C3 opsonization is independent of the sialylation state and of the oligosaccharide determinant of gonococcal **lipooligosaccharide** (**LOS**). Quantitative association/invasion assays performed in the presence or absence of **LOS** competimers support C3b deposition upon the lipid A core structure. Our findings demonstrate a role for lipid A as a C3 acceptor site and suggest that multiple factors govern C3b deposition and its subsequent conversion to iC3b on the surface of the gonococcus.

Quantitative adherence and invasion inhibition assays suggest that iC3b covalently **bound** to the gonococcus serves as a primary ligand for CR3. Gonococcal porin and **pilin** can also **bind** to the I-domain in a non-opsonic manner and are required for the gonococcus-CR3 association. Although Opa proteins are not required for initiation of gonococcal cervicitis, they may play a role in potentiating infection. Collectively, our data suggest that opsonic and non-opsonic gonococcal adherence to CR3 occurs in a cooperative manner that facilitates targeting to and successful invasion of the cervical epithelium. iC3b-dependent, CR3-mediated endocytosis occurs independently of a proinflammatory response and is consistent with the asymptomatic nature of N. gonorrhoeae infection in women.

L42 ANSWER 3 OF 20 BIOSIS
ACCESSION NUMBER: 2002:585019 BIOSIS
DOCUMENT NUMBER: PREV200200585019
TITLE: Opsonic and non-opsonic interactions occur between

Neisseria gonorrhoeae and complement receptor 3 on primary cervical epithelial cells.

AUTHOR(S): Edwards, J. L. [Reprint author]; Brown, E. J.; Uk-Nham, S.; Cannon, J. G.; Blake, M. S.; **Apicella, M. A.** [Reprint author]

CORPORATE SOURCE: University of Iowa, Iowa City, IA, USA

SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2002) Vol. 102, pp. 93. print.
Meeting Info.: 102nd General Meeting of the American Society for Microbiology. Salt Lake City, UT, USA. May 19-23, 2002. American Society for Microbiology.
ISSN: 1060-2011.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 13 Nov 2002
Last Updated on STN: 13 Nov 2002

AB Little is known about the pathogenesis of gonococcal infection within the lower female genital tract. We recently described the distribution of complement receptor 3 (CR3) within epithelia derived from the female genital tract. CR3-mediated endocytosis was subsequently demonstrated to serve as a primary mechanism by which N. gonorrhoeae elicits membrane ruffling and cellular invasion of primary, human, cervical epithelial cells. We have extended these studies to describe the nature of the gonococcus-CR3 interaction. Western Blot analysis demonstrates production of alternative complement components by ecto- and endocervical cells, which allows C3b deposition on gonococcal lipooligosaccharide (**LOS**) and its rapid conversion to iC3b. C3 opsonization is independent of the **LOS** sialylation state and of oligosaccharide side chain length. Quantitative adherence and invasion inhibition assays suggest that iC3b covalently **bound** to the gonococcus serves as a primary ligand for CR3 adherence, since recombinant I-domain and anti-iC3b and -factor I antibodies significantly inhibit adherence and invasion of primary ecto- and endocervical cells. However, gonococcal porin and **pili** can also **bind** to the I-domain of CR3 in a non-opsonic manner as demonstrated by ELISA and Western Blot analysis. The association of the gonococcus with CR3 requires por and pil **outer membrane proteins**. Although Opa proteins are not required for initiation of gonococcal cervicitis, they may play a role in potentiating infection. Collectively, these data suggest that opsonic and non-opsonic gonococcal adherence to CR3 occurs in a cooperative manner that facilitates targeting to and successful invasion of the cervical epithelium.

L42 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2001:166569 HCAPLUS
DOCUMENT NUMBER: 134:323382

TITLE: Construction of acetate auxotrophs of Neisseria meningitidis to study host-meningococcal **endotoxin** interactions

AUTHOR(S): Giardina, Peter C.; Gioannini, Theresa; Buscher, Benjamin A.; Zaleski, Anthony; Zheng, De-Shang; Stoll, Lynn; Teghanemt, Athmane; **Apicella,**

Michael A.; Weiss, Jerrold
CORPORATE SOURCE: Department of Microbiology, Division of Infectious Diseases, The Inflammation Program, University of Iowa and Veterans' Administration Medical Center, Iowa City, IA, 52242, USA
SOURCE: Journal of Biological Chemistry (2001), 276(8), 5883-5891
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To facilitate studies of the mol. determinants of host-meningococcal **lipooligosaccharide** (**endotoxin**) interactions at patho-physiol. relevant **endotoxin** concns. (i.e., ≤10 ng/mL), the authors have generated acetate auxotrophs NMBACE1 from encapsulated Neisseria meningitidis (serogroup B, strain NMB) and NMBACE2 from an isogenic bacterial mutant lacking the polysialic acid capsule. Growth of the auxotrophs in medium containing [14C]acetate yielded 14C-**lipooligosaccharides** containing .apprx.600 cpm/ng. Gel sieving resolved 14C-**lipooligosaccharide**-containing aggregates with an estimated mol. mass of ≥20 + 106 Da (peak A) and .apprx.1 + 106 Da (peak B) from both strains. **Lipooligosaccharides** in peaks A and B had the same fatty acid composition and SDS-polyacrylamide gel electrophoresis profile. 14C-Labeled capsule copurified with 14C-**lipooligosaccharides** in peak B from NMBACE1, whereas the other aggregates contained only 14C-**lipooligosaccharide**. For all aggregates, **lipopolysaccharide-binding** protein and soluble CD14-induced delivery of **lipooligosaccharides** to endothelial cells and cell activation correlated with disaggregation of **lipooligosaccharides**. These processes were inhibited by the presence of capsule but unaffected by the size of the aggregates. In contrast, **endotoxin** activation of cells containing membrane CD14 was unaffected by capsule but diminished when **endotoxin** was presented in larger aggregates. These findings demonstrate that the phys. presentation of **lipooligosaccharide**, including possible interactions with capsule, affect the ability of meningococcal **endotoxin** to interact with and activate specific host targets.
REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2001:604742 HCAPLUS
DOCUMENT NUMBER: 135:316689
TITLE: **Binding** of the non-typeable Haemophilus influenzae **lipooligosaccharide** to the PAF receptor initiates host cell signalling
AUTHOR(S): Swords, W. Edward; Ketterer, Margaret R.; Shao, Jianqiang; Campbell, Colleen A.; Weiser, Jeffrey N.; **Apicella, Michael A.**
CORPORATE SOURCE: Department of Microbiology, University of Iowa,

Iowa City, IA, 52242, USA
SOURCE: Cellular Microbiology (2001), 3(8), 525-536
CODEN: CEMIF5; ISSN: 1462-5814
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Non-typeable Haemophilus influenzae (NTHi) invades host cells by **binding** of the platelet-activating factor (PAF) receptor via **lipooligosaccharide** (**LOS**) glycoforms containing phosphorylcholine (ChoP). The effect of NTHi infection on host cell signaling and its role in NTHi invasion was examined The infection of human bronchial epithelial cells with NTHi 2019 increased cytosolic Ca2+ levels, and the invasion of bronchial cells by NTHi 2019 was inhibited by pretreatment with the cell-permeant intracellular Ca2+ chelator BAPTA-AM ($P = 0.022$) or thapsigargin ($P = 0.016$). Cytosolic inositol phosphate (IP) levels were also increased after infection with NTHi 2019 ($P < 0.001$), but not after infection with isogenic mutants expressing altered **LOS** glycoforms lacking ChoP. PAF receptor antagonist reduced NTHi 2019-stimulated IP production in a dose-dependent manner. NTHi 2019 invasion was inhibited by pertussis **toxin** (PTX) and the phosphatidylinositol-3-kinase inhibitors wortmannin and LY294002. The less invasive strain NTHi 7502 also initiated IP production, but was unaffected by PAF receptor antagonist or PTX. These data demonstrate that the **binding** of the PAF receptor by NTHi initiates receptor coupling to a PTX-sensitive heterotrimeric G protein complex, resulting in a multifactorial host cell signal cascade and bacterial invasion. Moreover, the data suggest that NTHi strains initiate cell signaling and invade by different mechanisms, and that invasion mediated by PAF receptor activation is more efficient than macropinocytosis.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 6 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 1999:597423 HCAPLUS
DOCUMENT NUMBER: 131:213104

TITLE: Antigenic **conjugates** of conserved **lipopolysaccharides** of gram negative bacteria

INVENTOR(S): **Arumugham, Rasappa G.; Fortuna-Nevin, Maria; Apicella, Michael A.; Gibson, Bradford W.**
PATENT ASSIGNEE(S): American Cyanamid Company, USA

SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 941738	A1	19990915	EP 1999-301747	19990309

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,

PT, IE, SI, LT, LV, FI, RO

CA 2264970	AA	19990910	CA 1999-2264970	19990308
AU 9919540	A1	19990923	AU 1999-19540	19990309
AU 766184	B2	20031009		
JP 11322793	A2	19991124	JP 1999-61354	19990309
BR 9902008	A	20000509	BR 1999-2008	19990309

PRIORITY APPLN. INFO.: US 1998-37529 A 19980310

AB Antigenic **conjugates** are provided which comprise a carrier protein covalently **bonded** to the conserved portion of a **lipopolysaccharide** of a gram neg. bacteria, wherein said conserved portion of the **lipopolysaccharide** comprises the inner core and lipid A portions of said **lipopolysaccharide** , said **conjugate** eliciting a cross reactive immune response against heterologous strains of said gram neg. bacteria. The carrier protein is selected from CRM197, tetanus **toxin** , diphtheria **toxin**, pseudomonas exotoxin A, cholera **toxin**, group A streptococcal **toxin**, **pneumolysin** of Streptococcus pneumoniae, **filamentous hemagglutinin** (**FHA**), **FHA** of Bordetella pertussis, **pili** or **pilins** of Neisseria gonorrhoeae or meningitidis, **outer membrane proteins** of Neisseria meningitidis, **C5A peptidase** of Streptococcus and **surface protein** of Moraxella catarrhalis.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 7 OF 20 JAPIO (C) 2004 JPO on STN

ACCESSION NUMBER: 1999-322793 JAPIO

TITLE: ANTIGEN ZYGOTE CONSISTING OF PRESERVATIVE LIPOPOLYSACCHARIDE OF GRAM NEGATIVE BACTERIUM

INVENTOR: **ARUMUGHAM RASAPPA G; FORTUNA-NEVIN MARIA; APICELLA MICHAEL A; GIBSON BRADFORD W**

PATENT ASSIGNEE(S): AMERICAN CYANAMID CO

PATENT INFORMATION:

PATENT NO	KIND	DATE	ERA	MAIN IPC
JP 11322793	A	19991124	Heisei	C07K014-34

APPLICATION INFORMATION

STN FORMAT:	JP 1999-61354	19990309
ORIGINAL:	JP11061354	Heisei

PRIORITY APPLN. INFO.: US 1998-37529 19980310

SOURCE: PATENT ABSTRACTS OF JAPAN (CD-ROM), Unexamined Applications, Vol. 1999

AN 1999-322793 JAPIO

AB PROBLEM TO BE SOLVED: To obtain an antigen zygote inducing not only an immunogenic response against a specified species of a gram negative bacterium but also a cross reaction immune response against a different strain or a different serum type from that of a gram negative bacterium belonging to a specified genus, preferably against a gram negative bacterium of a different genus, and a vaccine containing the antigen zygote.

SOLUTION: The antigen zygote comprising a carrier protein bound by a covalent bond to a preservative part consisting of an inside core part and a lipid A part of lipopolysaccharide of a gram negative bacterium and a vaccine containing the antigen zygote. This antigen zygote induces a cross reaction immune response against a different strain of the gram negative bacterium, and preferably, against a gram negative bacterium of a different genus.

L42 ANSWER 8 OF 20 HCAPLUS
ACCESSION NUMBER: 1998:800024 HCAPLUS
DOCUMENT NUMBER: 130:51336
TITLE: Laft mutants of pathogenic gram-negative bacteria
INVENTOR(S): **Apicella, Michael A.; Gibson, Bradford W.**; Nichols, Wade A.
PATENT ASSIGNEE(S): University of Iowa Research Foundation, USA; University of California
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9853851	A1	19981203	WO 1998-US10881	19980528
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9877010	A1	19981230	AU 1998-77010	19980528

PRIORITY APPLN. INFO.: US 1997-47791P P 19970528
WO 1998-US10881 W 19980528

AB A method is provided for identifying, isolating, and producing **lipooligosaccharide** (**LOS**) mutants of gram-neg. bacterial pathogens. The method comprises mutating the laft gene of a gram-neg. bacterial pathogen so that there is a lack of a functional Lipid A fatty acid transferase protein. The resulting **LOS** mutants lack one or more secondary acyl chains as compared to the **LOS** contained in the wild type gram-neg. bacterial pathogen. The **LOS** isolated from the laft mutants displays substantially reduced toxicity as compared to that of the wild type strain. Also, the present invention provides methods for using a vaccine formulation containing the laft mutants, the **endotoxin** isolated therefrom, or the **endotoxin** isolated therefrom which is then **conjugated** to a carrier protein, to immunize an individual against infections caused by gram-neg. bacterial pathogens by administering a prophylactically effective amount of the vaccine formulation.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 1998:130782 HCAPLUS
DOCUMENT NUMBER: 128:256264
TITLE: Nonopsonic phagocytosis of group C Neisseria meningitidis by human neutrophils
AUTHOR(S): Estabrook, Michele M.; Zhou, Daoguo; **Apicella, Michael A.**
CORPORATE SOURCE: Department of Pediatrics, Case Western Reserve University School of Medicine, Cleveland, OH, USA
SOURCE: Infection and Immunity (1998), 66(3), 1028-1036
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Although complement-mediated bactericidal activity in serum has long been known to be very important in host defense against Neisseria meningitidis, recent studies have shown that opsonic phagocytosis by neutrophils is also important. The purpose of this study was to determine if endemic group C N. meningitidis strains were susceptible to non-opsonic (complement- and antibody-independent) phagocytosis by human neutrophils, which is a well-described phenomenon for Neisseria gonorrhoeae. Gonococci that possess one or more of a group of heat-modifiable **outer membrane proteins** (called opacity-associated [Opa] proteins) are phagocytosed by neutrophils in the absence of serum. The authors found that four serogroup C meningococcal strains bearing the lacto-N-neotetraose (LNnT) structure on **lipooligosaccharide** (**LOS**) were phagocytosed by neutrophils in the absence of antibody and active complement. Confocal microscopy confirmed that the organisms were internalized by neutrophils. This susceptibility was not restricted to carrier isolates, since two of the strains were cultured from blood or cerebrospinal fluid. All four strains expressed Opa protein and had relatively less endogenous **LOS** and capsule sialylation compared to six strains that were resistant to this type of phagocytosis. Non-opsonic phagocytosis of two of the four strains was inhibited by exogenous sialylation of **LOS** LNnT and the **binding** of monoclonal antibody to LNnT. However, an isogenic mutant that lacked the LNnT structure was fully susceptible to non-opsonic phagocytosis. The authors conclude that group C meningococci can be phagocytosed by neutrophils in the absence of antibody and active complement possibly by two different mechanisms. Expression of Opa protein and downregulation of endogenous surface sialic acids analogous to what is seen for N. gonorrhoeae might be necessary for N. meningitidis as well.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 10 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 1997:496805 HCAPLUS

DOCUMENT NUMBER: 127:107983
TITLE: Non-toxic mutants of pathogenic gram-negative bacteria
INVENTOR(S): **Apicella, Michael A.**; Sunshine, Melvin G.; Lee, Na-gyong; **Arumugham, Rasappa**; **Gibson, Bradford W.**
PATENT ASSIGNEE(S): University of Iowa Research Foundation, USA; The Regents of the University of California; American Cyanamid Company; Apicella, Michael A.; Sunshine, Melvin G.; Lee, Na-Gyong; Arumugham, Rasappa; Gibson, Bradford W.
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9719688	A1	19970605	WO 1996-US18984	19961127
W: AU, CA, JP, KR, MX, NZ, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2238640	AA	19970605	CA 1996-2238640	19961127
CA 2238640	C	20020917		
AU 9711246	A1	19970619	AU 1997-11246	19961127
AU 710933	B2	19990930		
EP 876150	A1	19981111	EP 1996-942080	19961127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001500363	T2	20010116	JP 1997-520648	19961127

PRIORITY APPLN. INFO.: US 1995-565943 A 19951201
WO 1996-US18984 W 19961127

AB A method is provided for identifying, isolating, and producing htrB mutants of gram-neg. bacterial pathogens. The method comprises mutating the htrB gene of a gram-neg. bacterial pathogen so that there is a lack of a functional htrB protein, resulting in a mutant that lacks ≥1 secondary acyl chains contained in the wild type gram-neg. bacterial pathogen, and displays substantially reduced toxicity as compared to the wild type strain. The present invention also provides methods for using a vaccine formulation containing the htrB mutant, the endotoxin isolated therefrom, or the endotoxin isolated therefrom which is then conjugated to a carrier protein to immunize an individual against infections caused by gram-neg. bacterial pathogens by administering a prophylactically effective amount of the vaccine formulation.

L42 ANSWER 11 OF 20 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 7
ACCESSION NUMBER: 1997:515443 BIOSIS
DOCUMENT NUMBER: PREV199799814646
TITLE: Phase variation and conservation of **lipooligosaccharide** epitopes in Haemophilus somnus.

Searcher : Shears 571-272-2528

AUTHOR(S): Inzana, Thomas J. [Reprint author]; Hensley, Jennifer; McQuiston, John; Lesse, Alan J.; Campagnari, Anthony A.; Boyle, Stephen M.; **Apicella, Michael A.**

CORPORATE SOURCE: Cent. Mol. Med. Infect. Dis., Virginia-Maryland Regional Coll. Vet. Med., Virginia Polytechnic Inst. State Univ., Blacksburg, VA, USA

SOURCE: Infection and Immunity, (1997) Vol. 65, No. 11, pp. 4675-4681.
CODEN: INFIBR. ISSN: 0019-9567.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 10 Dec 1997
Last Updated on STN: 10 Dec 1997

AB The bovine-specific pathogen Haemophilus somnus is capable of undergoing structural and antigenic phase variation in its **lipooligosaccharide** (**LOS**) components after in vivo and in vitro passage. However, commensal isolates from the reproductive tract have not been observed to vary in phase (T. J. Inzana, R. P. Gogolewski, and L. B. Corbeil, Infect. Immun. 60:2943-2951, 1992). We now report that specific monoclonal antibodies (MAbs) to the LOSs of Haemophilus aegyptius, Neisseria gonorrhoeae, and Haemophilus influenzae, as well as H. somnus, reacted with some phase-variable epitopes in H. somnus **LOS** . All reactive MAbs **bound** to **LOS** components of about 4.3 kDa in the same H. somnus isolates, including a non-phase-varying strain. Following in vitro passage of a clonal variant of strain 738 that was nonreactive with the MAbs, 11.8% of young colonies shifted to a reactive phenotype. A digoxigenin-labelled 5'-CAATCAATCAATCAATCAATCAATCAAT-3' oligo-nucleotide probe hybridized to genomic DNA from strain 738 but did not react with DNA from a non-phase-varying strain. Sequence analysis of the gene containing 5'-CAAT-3' tandem sequences revealed 48% amino acid homology with the lex-2B gene-encoded protein of H. influenzae type b. Our results indicate that some **LOS** epitopes are conserved between H. somnus and other Haemophilus and Neisseria species, that **LOS** phase variation may occur at a high rate in some strains of H. somnus, and that phase variation may, in part, be due to 5'-CAAT-3' tandem sequences present in H. somnus genes.

L42 ANSWER 12 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 8

ACCESSION NUMBER: 1995:593605 HCAPLUS

DOCUMENT NUMBER: 123:30562

TITLE: A **lipooligosaccharide-binding** site on HepG2 cells similar to the gonococcal opacity-associated **surface protein** Opa

AUTHOR(S): Porat, N.; **Apicella, M. A.**; Blake, M. S.

CORPORATE SOURCE: Laboratory of Bacterial Pathogenesis and Immunology, The Rockefeller University, New York, NY, 10021, USA

SOURCE: Infection and Immunity (1995), 63(6), 2164-72
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal
LANGUAGE: English

AB The lacto-N-neotetraose-containing **lipooligosaccharide** (**LOS**) present on the surface of most Neisseria gonorrhoeae organisms may serve many important functions in gonococcal pathogenesis. This surface glycolipid contains the cross-reactive epitope to human paragloboside and can be sialylated by gonococci grown in the presence of CMP-N-acetylneuraminic acid. Another possible role for this glycolipid could be to mimic human asialocarbohydrates and act as a ligand for asialoglycoprotein receptors contained on numerous human cells. The most noted of this large family of receptors is that expressed on the surface of hepatic cells. In a model cell system, using the hepatoma tissue culture cell line HepG2, the authors wanted to investigate if the presence of this asialoglycoprotein receptor influenced the adherence and/or invasion of gonococci expressing the lacto-N-neotetraose structure. Piliated variants of the gonococcal wild-type strain 1291 and its isogeneic **LOS** mutant 1291E were used in adherence-invasion assays. This gonococcal strain is somewhat unusual in that it expresses large amts. of predominantly one species of **LOS**, thus reducing the complexity of interpreting the data. The data from these assays suggested that the Gal(β1-4)GlcNAc(β1-3)Gal(β1-4)Glc carbohydrate structure on the wild-type **LOS** affected the adherence-invasion of gonococci into the HepG2 cells. In studies to determine whether the major hepatic asialoglycoprotein receptor was involved in these interactions, the authors found that the HepG2 cells contained two receptors which **bound** gonococcal **LOS**. One of these was the asialoglycoprotein receptor, and the data concerning this receptor will be reported elsewhere. The data on the second receptor are reported here. Purified, 125I-labeled gonococcal **LOS** was used to identify specific high-affinity **LOS-binding** sites. These **binding** expts. revealed one major **binding** site corresponding to a protein with a mol. mass of 70 kDa (p70). Several lines of evidence in this study suggested that the oligosaccharide region of **LOS** played an important role in **LOS binding** to the p70 of HepG2 cells. In addition, the authors show that this human **LOS** receptor has some similarities to the gonococcal Opa proteins.

L42 ANSWER 13 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 9
ACCESSION NUMBER: 1992:229609 HCAPLUS
DOCUMENT NUMBER: 116:229609
TITLE: Role of the rfaG and rfaP genes in determining the **lipopolysaccharide** core structure and cell surface properties of Escherichia coli K-12
AUTHOR(S): Parker, Craig T.; Kloser, Andrew W.; Schnaitman, Carl A.; Stein, Murry A.; Gottesman, Susan; **Gibson, Bradford W.**
CORPORATE SOURCE: Dep. Microbiol., Arizona State Univ., Tempe, AZ, 85287, USA
SOURCE: Journal of Bacteriology (1992), 174(8), 2525-38
CODEN: JOBAAY; ISSN: 0021-9193
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Deletions which removed rfa genes involved in **lipopolysaccharide** (**LPS**) core synthesis were constructed in vitro and inserted into the chromosome by linear transformation. The deletion Δrfa1, which removed rfaGPBI, resulted in a truncated **LPS** core containing two heptose residues but no hexose and a deep rough phenotype including decreased expression of major **outer membrane proteins**, hypersensitivity to novobiocin, and resistance to phage U3. In addition, Δrfa1 resulted in the loss of flagella and **pili** and a mucoid colony morphol. Measurement of the synthesis of β-galactosidase from a cps-lacZ fusion showed that the mucoid phenotype was due to rcsC-dependent induction of colanic acid capsular polysaccharide synthesis. Complementation of Δrfa1 with rfaG+ DNA fragments resulted in a larger core and restored the synthesis of flagella and **pili** but did not reverse the deep rough phenotype or the induction of cps-lacZ, while complementation with a fragment carrying only rfaP+ reversed the deep rough phenotype but not the loss of flagella and **pili** . A longer deletion which removed rfaQGPBIJ was also constructed, and complementation studies with this deletion showed that the product of rfaQ was not required for the functions of rfaG and rfaP. Thus, the function of rfaQ remains unknown. Tandem mass spectrometric anal. of **LPS** core oligosaccharides from complemented Δrfa1 strains indicated that rfaP+ was necessary for the addition of either phosphoryl (P) or pyrophosphorylethanolamine (PPEA) substituents to the heptose I residue, as well as for the partial branch substitution of heptose II by heptose III. The substitution of heptose II is independent of the type of P substituent present on heptose I, and this results in four different core structures. A model is presented which relates the deep rough phenotype to the loss of heptose-**linked** P and PPEA.

L42 ANSWER 14 OF 20 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 91187057 EMBASE
DOCUMENT NUMBER: 1991187057
TITLE: Endogenous sialylation of the **lipooligosaccharides** of Neisseria meningitidis.
AUTHOR: Mandrell R.E.; Kim J.J.; John C.M.; **Gibson B.W.**; Sugai J.V.; **Apicella M.A.**; Griffiss J.M.; Yamasaki R.
CORPORATE SOURCE: Center for Immunochemistry, Veterans Admin. Medical Center, 4150 Clement Street,San Francisco, CA 94121, United States
SOURCE: Journal of Bacteriology, (1991) 173/9 (2823-2832). ISSN: 0021-9193 CODEN: JOBAAY
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Monoclonal antibodies (MAb) 3F11 and 06B4 recognize epitopes that are conserved on gonococcal **lipooligosaccharides** (**LOS**), present on some meningococcal **LOS**, and

conserved on human erythrocytes. **LOS** of some group B and C prototype meningococcal **LOS** strains (**LOS** serotypes L1 to L8) treated with neuraminidase showed increased expression of the 3F11 and 06B4 MAb-defined epitopes. Neuraminidase-treated **LOS** separated by sodium dodecyl sulfate-polyacrylamide gel electrophoresis and silver stained showed a shift in migration from a component with a mass of approximately 4.8 kDa to a component with a mass of between 4.5 and 4.6 kDa. The same strains grown in medium with excess CMP-N-acetylneuraminic acid had **LOS** that shifted in migration to a slightly higher component (mass, approximately 4.8 kDa). Chemical analysis of the neuraminidase-digested products from one **LOS** indicated it contained approximately 1.5% sialic acid. Covalent **linkage** between sialic acid and the **LOS** was confirmed by analysis of de-O-acylated and dephosphorylated **LOS** by liquid secondary ion mass spectrometry. These studies show that some meningococci contain sialic acid in their **LOS**, that the sialic acid is cleaved and lost in conventional acetic acid hydrolysis, and that the sialic acid alters the expression of MAb-defined epitopes.

L42 ANSWER 15 OF 20 DISSABS COPYRIGHT (C) 2004 ProQuest Information and Learning Company; All Rights Reserved on STN

ACCESSION NUMBER: 90:6124 DISSABS Order Number: AAR9022162
TITLE: PRODUCTION AND CHARACTERIZATION OF NEISSERIA GONORRHOEAE OLIGOSACCHARIDE-PROTEIN **CONJUGATES**
AUTHOR: HANES, DARCY ELIZABETH [PH.D.]; **APICELLA, MICHAEL [advisor]**
CORPORATE SOURCE: STATE UNIVERSITY OF NEW YORK AT BUFFALO (0656)
SOURCE: Dissertation Abstracts International, (1990) Vol. 51, No. 3B, p. 1107. Order No.: AAR9022162. 176 pages.
DOCUMENT TYPE: Dissertation
FILE SEGMENT: DAI
LANGUAGE: English
ENTRY DATE: Entered STN: 19921118
Last Updated on STN: 19921118

AB Several outer membrane components of Neisseria gonorrhoeae, such as proteins II and **pili**, have been evaluated by other researchers as vaccine candidates with limited success. This work proposes to study the oligosaccharide (OS) portion of **LOS** **conjugated** to tetanus **toxoid**, **pilin**, and an oligopeptide derived from **pilin** as potential vaccines.

Lipooligosaccharide (**LOS**) from Neisseria gonorrhoeae strain 8 was selectively hydrolyzed with 1% acetic acid to release oligosaccharide from lipid A. This OS was **conjugated** to one of three protein carriers, **tetanus toxoid** (**TT**), **pili**, and a common oligopeptide from gonococcal **pilin** termed TC-2. The **TT**-OS **conjugate** was composed of approximately 4.5% OS and 45% **TT**, and had a M$\sb{\rm r}$ of $>$200,000 daltons. The **pilin**-OS **conjugate** was composed of approximately 22% OS and 80% **pili** and had a M$\sb{\rm r}$ of approximately 22,000 daltons, while the TC-2-OS **conjugate** was approximately 45% TC-2 and 55% OS with a M$\sb{\rm r}$< 14,000 daltons.

Mice immunized with 25.0 ug, 10.0 ug or 1.0 ug of the TT-OS **conjugate** demonstrated anti-**LOS** antibodies to titers of 1:3200, 1:400, and 1:400 respectively. Conversely, the **pilin**-OS **conjugate** elicited **LOS** antibodies at doses of 1.0 ug and 2.5 ug with titers of 1:3200 and 1:6400 respectively. The TC-2-OS **conjugate** demonstrated no ability to elicit anti-**LOS** antibodies above control levels.

Immunization with 1.0 ug of the **pilin**-OS **conjugate** elicited serum IgM antibodies to **LOS** by day 5, IgM then fell to background by day 21, and did not significantly increase after a booster immunization. In contrast, IgG was detectable by day 5, and exhibited a two fold increase above controls following a booster immunization.

The bactericidal activity of **pili**-OS and TT-OS antisera were examined against homologous strain 8. Antiserum to the TT-OS **conjugate** demonstrated a maximum killing of 61.58% at dilution of 1:100, while antiserum to the **pili**-OS **conjugate** showed 98.17% killing at 1:100. Against 3 heterologous strains of the same serotype, antiserum to the TT-OS **conjugate** only killed strain 3027 (61.58%), while antiserum to the **pili**-OS **conjugate** killed strains 2431 (74.94%), and 2586 (70.45%). One strain with a heterologous serotype, 2687, was also tested and only antiserum to the **pili**-OS **conjugate** demonstrated killing (52.57%) against this strain.

These data demonstrate that anti-**LOS** antibodies are elicited by protein-oligosaccharide **conjugates**. These antibodies do exhibit bactericidal activity against N. gonorrhoeae. However, there may be differences in antigenic expression of the oligosaccharide on different carrier molecules.

L42 ANSWER 16 OF 20 MEDLINE on STN

ACCESSION NUMBER:	89183402 MEDLINE
DOCUMENT NUMBER:	PubMed ID: 2648296
TITLE:	Somatic antigens of Haemophilus influenzae as vaccine components.
AUTHOR:	Murphy T F; Campagnari A A; Nelson M B; **Apicella M A**
CORPORATE SOURCE:	Department of Medicine, School of Medicine, State University of New York, Buffalo.
CONTRACT NUMBER:	AI19641 (NIAID)
SOURCE:	Pediatric infectious disease journal, (1989 Jan) 8 (1 Suppl) S66-8. Ref: 20 Journal code: 8701858. ISSN: 0891-3668.
PUB. COUNTRY:	United States
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE) General Review; (REVIEW) (REVIEW, TUTORIAL)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	198904
ENTRY DATE:	Entered STN: 19900306 Last Updated on STN: 19970203 Entered Medline: 19890421

L42 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 10
ACCESSION NUMBER: 1987:31086 HCAPLUS
DOCUMENT NUMBER: 106:31086
TITLE: Immunity to Haemophilus influenzae type b in young adults: correlation of bactericidal and opsonizing activity of serum with antibody to polyribosylribitol phosphate and **lipooligosaccharide** before and after vaccination
AUTHOR(S): Musher, Daniel; Goree, Allen; Murphy, Timothy; Chapman, Alan; Zahradnik, John; **Apicella, Michael**; Baughn, Robert
CORPORATE SOURCE: V.A. Med. Cent., Baylor Coll. Med., Houston, TX, 77211, USA
SOURCE: Journal of Infectious Diseases (1986), 154(6), 935-43
CODEN: JIDIAQ; ISSN: 0022-1899
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Naturally acquired humoral immunity is thought to protect adults against serious infections due to H. influenzae type b (Hib). Antibody to the polyribosylribitol phosphate (PRP) capsule is generally considered protective; antibody to **lipooligosaccharide** (**LOS**) or **outer membrane protein** (**OMP**) may also play a role. Serum from 23 of 50 healthy young adults had no bactericidal effect (BE) against Hib yet opsonized these organisms for .apprx.30% uptake by polymorphonuclear leukocytes. The degree of bactericidal and opsonizing activity in serum from the other 27 subjects generally correlated with the level of antibody to PRP but not to **LOS** or **OMP**. However, serum from some individuals had levels of antibody to PRP as high as 4.9 μg/mL without BE, and 7 of 27 subjects with BE had antibody levels of <1 μg/mL. After vaccination with 20 μg of **conjugated** PRP, the level of antibody to PRP was >5 μg/mL in all 50 subjects. BE appeared in 22 of those who originally lacked it, and opsonization increased to .apprx.50%.

L42 ANSWER 18 OF 20 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 86007018 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3876283
TITLE: Antigenic heterogeneity of **outer membrane proteins** of nontypable Haemophilus influenzae is a basis for a serotyping system.
AUTHOR: Murphy T F; **Apicella M A**
CONTRACT NUMBER: AI19641 (NIAID)
SOURCE: Infection and immunity, (1985 Oct) 50 (1) 15-21.
Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198510
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19970203

Searcher : Shears 571-272-2528

Entered Medline: 19851029

AB A serotyping system for nontypable Haemophilus influenzae (NTHI) was developed by using isolated **outer membrane protein** (**OMP**) preparations and rabbit antisera. **OMPs** of 23 strains were isolated by molecular sieve chromatography of outer membranes in 1.5% sodium deoxycholate buffer. These **OMP** preparations were relatively free of **lipopolysaccharide** as determined by silver staining of sodium dodecyl sulfate gels and by dot assay with a monoclonal antibody which is specific for the lipid A of H. influenzae. Three antisera raised to whole organisms were used to serotype 21 of 23 strains with a kinetic enzyme-**linked** immunosorbent assay. Digestion of **OMP** preparations with proteinase K removed greater than 90% of the antigenic reactivity, indicating that the system is based on **OMP** antigens. Marked antigenic heterogeneity of **OMPs** exists among strains of NTHI. By determining the pattern of serological reactivity of **OMPs** with the three antisera, isolates were divided into groups based on antigenic differences. Six serotypes were identified. This **OMP** serotyping system is based on multiple antigenic determinants. Future studies will focus on identifying serotype-specific epitopes to further refine this serological classification scheme for NTHI.

L42 ANSWER 19 OF 20 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 12

ACCESSION NUMBER: 1983:307509 BIOSIS
DOCUMENT NUMBER: PREV198376065001; BA76:65001
TITLE: **ENDO TOXIN** CONTAMINATION OF ENZYME **CONJUGATES** USED IN ENZYME **LINKED** IMMUNO SORBENT ASSAYS.
AUTHOR(S): BRYANT R E [Reprint author]; CHAMOVITZ B N; MORSE S A; **APICELLA M A**; MORTHLAND V H
CORPORATE SOURCE: DEP MED, OREGON HEALTH SCI UNIV, PORTLAND, OR 97201, USA
SOURCE: Journal of Clinical Microbiology, (1983) Vol. 17, No. 6, pp. 1050-1053.
CODEN: JCMIDW. ISSN: 0095-1137.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB The specificity of the enzyme-**linked** immunosorbent assay(s) [ELISA] is thought to depend on the specificity of the antibody used in the assay system. Therefore, the association of broadly reactive antigens like **endotoxin** with enzyme **conjugates** or other ELISA reagents has the potential of altering the specificity of reactions in the ELISA. Using the Limulus amoebocyte lysate assay, it was demonstrated that commercially prepared **conjugates** of goat anti-human IgG peroxidase, goat anti-rabbit IgG alkaline phosphatase, rabbit anti-human IgG and other enzyme **conjugates** contained **endotoxin**. The staphylococcal protein A, horseradish peroxidase and bovine alkaline phosphatase used to prepare enzyme **conjugates** also contained **endotoxin**. Commercially obtained bovine alkaline phosphatase contained as much as 1.0 μg of **endotoxin**/ml of enzyme solution. Commercially and

laboratory prepared enzyme **conjugates** contained **endotoxin** as determined by their absorption to immobilized monoclonal antibody to lipid A or to immobilized Limulus amoebocyte lysate. Thus, **endotoxin** was apparently associated with the enzyme component of the **conjugate.** In a competitive inhibition enzyme immunoassay, 10 μg of lipid A/ml inhibited **binding** of the enzyme **conjugate** to adsorbed Limulus amoebocyte lysate, thereby confirming that **endotoxin** mediated the **binding** of the **conjugate** in that system. The potential significance of **endotoxin bound** to enzyme **conjugates** may be far reaching because of the ubiquity of **endotoxin** in **conjugates** and the prevalence of antibodies to **endotoxin** in mammalian serum.

L42 ANSWER 20 OF 20 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 82099571 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6798135
TITLE: Isolation of a **lipopolysaccharide** mutant of Neisseria gonorrhoeae: an analysis of the antigenic and biologic difference.
AUTHOR: Morse S A; **Apicella M A**
CONTRACT NUMBER: AI-13571 (NIAID)
AI-16266 (NIAID)
AI-16267 (NIAID)
SOURCE: Journal of infectious diseases, (1982 Feb) 145 (2) 206-16.
Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198203
ENTRY DATE: Entered STN: 19900317
Last Updated on STN: 19970203
Entered Medline: 19820326

AB Analysis of the surface constituents of a pyocin 611 131-resistant variant of strain number JW-31 of Neisseria gonorrhoeae revealed substantial differences in the **lipopolysaccharide** (**LPS**) but not changes in the auxotype or **outer-membrane proteins.** Immunodiffusion and an enzyme-**linked** immunosorbent assay showed that the variant strain (number JW-31R) lost both the **LPS** serotype and the variable antigens while retaining at least a portion of the common determinant. The use of monoclonal antibody indicated that LPSs from strain number JW-31R and pyocin 611 131-resistant strains of other **LPS** serotypes lack a D-galactosaminyl-D-galactopyranosyl-D-glucose moiety. The **LPS**-derived polysaccharide from strain number JW-31 **binds** to wheat-germ lectin in precipitin and inhibition systems, whereas the JW-31R polysaccharide exhibits a markedly reduced affinity. In the presence of normal human serum, 99% of strain number JW-31R was killed within 20 min and strain number JW-31 was not.

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S3 9628 S2 AND (LOS OR LPS OR ENDOTOXIN? ? OR ENDO(W)TOXIN? ? OR LIPOPOLYSACCHARIDE? ? OR LIPOOLIGOSACCHARIDE? ? OR LIPO(W)(POLYSACCHARIDE? ? OR OLIGOSACCHARIDE? ? OR (POLY OR OLIGO)(W)SACCHARIDE? ?) OR (LIPOPOLY OR LIPOOLIGO)(W)SACCHARIDE? ?)
S4 228 S3 AND ((LC OR LONG(W)CHAIN)(W)SPDP OR SATA OR SATP OR SMCC OR MBS OR IS?ABI OR SMPB OR BANSI OR ADH OR EDAC OR DTSSP OR (ADIPIC OR ADIPOYL)(2W)(DIHYDRAZIDE OR DI(W)HYDRAZIDE) OR ADIPOYLDIHYDRAZIDE)
S5 170 S3 AND (SUCCIN?(10N)(MALEIMIDO? OR ACETYLTHIOACETATE OR (AC OR ACETYL)(W)(THIOACETATE OR THIO(W)ACETATE) OR ACETYLTHIO(W-)ACETATE) OR (MALEIMIDOBENZ? OR MALEIMIDO(W)BENZ?)(3W)(HYDROXYSUCCIN? OR HYDROXY(W)SUCCIN?) OR MALEIMIDOBENZOYLOXY...
S6 0 S S3 AND (ISLABI OR IS1ABI OR ISIABI OR (ETHYL OR ET)(5N)CARBODIIMIDE OR ETHYLCARBODIIMIDE)
S7 302 (S4 OR S5) AND (LINK? OR CONJUGAT? OR BOND OR BOUND OR BIND? OR BONDED OR CROSSLINK?)
S8 303 (S4 OR S5) AND (LINK? OR CONJUGAT? OR BOND OR BOUND OR BIND? ? OR BINDING OR BONDED OR CROSSLINK?)
S9 200 S8 AND COVALEN?
S10 187 S9 AND ANTIGEN?

S12 9 S10 AND (PEA OR PHOSPHOETHANOLAMINE OR PHOSPHO(W)(ETHANOLAMINE OR ETHANOL(W)AMINE) OR PHOSPHOETHANOL(W)AMINE)
S13 9 RD (unique items)
>>>No matching display code(s) found in file(s): 65, 113

13/3,AB/1 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
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01682603
Production in bacteria ad yeast of hemoglobin and analogues thereof
Herstellung von Hamoglobin und Analogen davon durch Bakterien und Hefen
Production d'hemoglobine et de ses analogues par des bacteries et chez la

levure
PATENT ASSIGNEE:
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PATENT (CC, No, Kind, Date): EP 1380645 A2 040114 (Basic)
APPLICATION (CC, No, Date): EP 2003077231 900510;
PRIORITY (CC, No, Date): US 349623 890510; US 374161 890630; US 379116 890713
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 700997 (EP 95110064)
EP 402300 (EP 90610036)
INTERNATIONAL PATENT CLASS: C12N-015/12; C07K-014/805; G01N-033/72; C12P-021/02

ABSTRACT EP 1380645 A2
A method of producing a hemoglobin-like protein wherein an alpha globin-like polypeptide and a beta globin-like polypeptide are each expressed in transformed non-erythrocyte cells such as bacterial or yeast cells, the method comprising expressing the alpha and beta globin-like polypeptide in the same cell in such manner that the alpha and beta globin-like polypeptides are assembled and combined with heme so as to intracellularly produce a biologically functional hemoglobin-like protein in soluble, recoverable form.
ABSTRACT WORD COUNT: 75
NOTE:
Figure number on first page: 1

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200403	1640
SPEC A	(English)	200403	34409
Total word count - document A			36049
Total word count - document B			0
Total word count - documents A + B			36049

13/3,AB/2 (Item 2 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01652181
HIV antisense proteins
HIV Antisense Proteine
Proteines antisens d' VIH

PATENT ASSIGNEE:
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LEGAL REPRESENTATIVE:
Taylor, Kathryn May et al (127471), Mathys & Squire, 100 Gray's Inn Road, London WC1X 8AL, (GB)
PATENT (CC, No, Kind, Date): EP 1359221 A2 031105 (Basic)
APPLICATION (CC, No, Date): EP 2003252743 030430;
PRIORITY (CC, No, Date): US 135545 020430
DESIGNATED STATES: AT; BE; BG; CH; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR; HU; IE; IT; LI; LU; MC; NL; PT; RO; SE; SI; SK; TR
EXTENDED DESIGNATED STATES: AL; LT; LV; MK
INTERNATIONAL PATENT CLASS: C12N-015/49; C07K-014/155; A61K-039/21; G01N-033/569
ABSTRACT EP 1359221 A2

Disclosed is a novel HIV gene comprising a set of open reading frames encoded with the template as the plus strand of the proviral DNA, and located in the region of HIV-1 long terminal repeat. The genes encode a set of antisense proteins, (HAPs) as well as smaller proteins, related to, and containing structural motif resembling that of chemokine proteins. Depending upon the ribosomal frameshift, a plurality of proteins may be translated from the antisense RNA. The smaller proteins have similarity with chemokine SDF-1 and may play a role as a cofactor with gp120 in the **binding** to and entry of HIV to a target cell.

ABSTRACT WORD COUNT: 107
NOTE:
Figure number on first page: 1

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200345	180
SPEC A	(English)	200345	18114
Total word count - document A			18294
Total word count - document B			0
Total word count - documents A + B			18294

13/3,AB/3 (Item 3 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01129188
CANCER TREATMENT METHODS USING THERAPEUTIC CONJUGATES THAT BIND TO AMINOPHOSPHOLIPIDS
KREBSBEHANDLUNG MIT AMINOPHOSPHOLIPIDE BINDENDEN, THERAPEUTISCHEN KONJUGATEN
PROCEDES DE TRAITEMENT DU CANCER METTANT EN APPLICATION DES CONJUGUES THERAPEUTIQUES SE FIXANT A DES AMINOPHOSPHOLIPIDES
PATENT ASSIGNEE:
BOARD OF REGENTS THE UNIVERSITY OF TEXAS SYSTEM, (266340), 201 West 7th Street, Austin, Texas 78701, (US), (Proprietor designated states: all)
INVENTOR:
THORPE, Philip, E., 6722 Lakewood, Dallas, TX 75214, (US)

RAN, Sophia, 5840 Spring Valley Road 1612, Dallas, TX 75240, (US)
BREKKEN, Rolf, A, 14304, 25th Avenue, Seattle, NE Washington 98125, (US)
LEGAL REPRESENTATIVE:
Gowshall, Jonathan Vallance (61531), FORRESTER & BOEHMERT
Pettenkoferstrasse 20-22, 80336 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1098665 A1 010516 (Basic)
EP 1098665 B1 030108
EP 1098665 B9 030813
WO 2000002587 000120
APPLICATION (CC, No, Date): EP 99935491 990712; WO 99US15668 990712
PRIORITY (CC, No, Date): US 92589 P 980713; US 110600 P 981202
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: A61K-047/48; A61K-049/04; A61K-049/00; A61K-051/10
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200333	2397
CLAIMS B	(German)	200333	2174
CLAIMS B	(French)	200333	3013
SPEC B	(English)	200333	61405
Total word count - document A			0
Total word count - document B			68989
Total word count - documents A + B			68989

13/3,AB/4 (Item 4 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01070801
Antigenic conjugates of conserved **lipopolysaccharides** of gram negative bacteria
Antigenkonjugate von konservierten **Lipopolysacchariden** aus gram-negativen Bakterien
Conjugues **antigeniques** de **lipopolysaccharides** de bacteries gram-negatives
PATENT ASSIGNEE:
American Cyanamid Company, (212598), Five Giralda Farms, Madison, New Jersey 07940-0874, (US), (Applicant designated States: all)
INVENTOR:
Arumugham, Rasappa G., 15 Elatia Circle Pittsford, New York 14534, (US)
Fortuna-Nevin, Maria, 696 Summit Drive, Webster, New York 14580, (US)
Apicella, Michael A., 2626 Johnson Crossing, Solon, Iowa 52333, (US)
Gibson, Bradford W., 1324 Peralta Avenue, Berkeley, California 94702, (US)
LEGAL REPRESENTATIVE:
Wileman, David Francis, Dr. et al (46002), c/o Wyeth Laboratories Huntercombe Lane South, Taplow Maidenhead Berkshire SL6 OPH, (GB)
PATENT (CC, No, Kind, Date): EP 941738 A1 990915 (Basic)
APPLICATION (CC, No, Date): EP 99301747 990309;
PRIORITY (CC, No, Date): US 37529 980310

DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: A61K-039/385; A61K-039/02; A61K-39:095

ABSTRACT EP 941738 A1
Antigenic conjugates are provided which comprise a carrier protein **covalently bonded** to the conserved portion of a **lipopolysaccharide** of a gram negative bacteria, wherein said conserved portion of the **lipopolysaccharide** comprises the inner core and lipid A portions of said **lipopolysaccharide**, said **conjugate** eliciting a cross reactive immune response against heterologous strains of said gram negative bacteria.
ABSTRACT WORD COUNT: 58
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	9937	707
SPEC A	(English)	9937	6253
Total word count - document A			6960
Total word count - document B			0
Total word count - documents A + B			6960

13/3,AB/5 (Item 5 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00999326
Thermal preactivation of gaseous precursor filled compositions
Thermische Voraktivierung von Zusammensetzungen mit einer Fullung bestehend aus gasformigen Vorlaufer
Preactivation thermique de compositions remplies d'un precurseur geaseux
PATENT ASSIGNEE:
IMARX PHARMACEUTICAL CORP., (2069730), 1635 East 18th Street, Tucson, AZ 85749, (US), (applicant designated states: AT;BE;CH;CY;DE;DK;ES;FI;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
Unger, Evan C., 13365 East Camino, La Cebadilla, Tucson, Arizona 85749, (US)
LEGAL REPRESENTATIVE:
James, Anthony Christopher W.P. et al (78471), Carpmaels & Ransford 43 Bloomsbury Square, London WC1A 2RA, (GB)
PATENT (CC, No, Kind, Date): EP 901793 A1 990317 (Basic)
APPLICATION (CC, No, Date): EP 98307421 980914;
PRIORITY (CC, No, Date): US 929847 970915
DESIGNATED STATES: DE; ES; FR; GB; IT
INTERNATIONAL PATENT CLASS: A61K-049/00; A61K-041/00;
ABSTRACT EP 901793 A1
The present invention describes, among other things, the surprising discovery that gaseous precursor filled compositions are profoundly more effective as acoustically active contrast agents when they are thermally preactivated to temperatures at or above the boiling point of the

instilled gaseous precursor prior to their in vivo administration to a patient. Further optimization of contrast enhancement is achieved by administering the gaseous precursor filled compositions to a patient as an infusion. Enhanced effectiveness is also achieved for ultrasound mediated targeting and drug delivery.
ABSTRACT WORD COUNT: 84

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	9911	1390
SPEC A	(English)	9911	51117
Total word count - document A			52507
Total word count - document B			0
Total word count - documents A + B			52507

13/3,AB/6 (Item 6 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00807119
HAPTEN-CARRIER **CONJUGATES** FOR USE IN DRUG-ABUSE THERAPY
HAPTEN-TRAGER-KONJUGATE ZUR ANWENDUNG IN DER DROGEN-MISSBRAUCHS-THERAPIE
CONJUGUES VECTEURS DE HAPTENE UTILISES DANS UNE THERAPIE CONTRE L'USAGE DE DROGUES
PATENT ASSIGNEE:
Xenova Research Limited, (4352290), 957 Buckingham Avenue, Slough, Berkshire SL1 4NL, (GB), (Proprietor designated states: all)
INVENTOR:
SWAIN, Philip, A., 51 Garden Street 1, Boston, MA 02114, (US)
SCHAD, Victoria, C., 105 Chestnut Street, Cambridge, MA 02139, (US)
GREENSTEIN, Julia, L., 174 Mount Vernon Street, West Newton, MA 02165, (US)
EXLEY, Mark, A., 201 Reservoir Road, Chestnut Hill, MA 02167, (US)
FOX, Barbara, S., 26 Pemberton Road, Wayland, MA 01778, (US)
POWERS, Stephen, P., 2008 Stearns Hill Road, Waltham, MA 02154, (US)
GEFTER, Malcolm, L., 46 Baker Bridge Road, Lincoln, MA 01773, (US)
BRINER, Thomas, J., 438 Appleton Street, Arlington, MA 02174, (US)
LEGAL REPRESENTATIVE:
Duckworth, Timothy John et al (75911), J.A. Kemp & Co., 14 South Square, Gray's Inn, London WC1R 5JJ, (GB)
PATENT (CC, No, Kind, Date): EP 814843 A2 980107 (Basic)
EP 814843 B1 031126
WO 96030049 961003
APPLICATION (CC, No, Date): EP 96910595 960327; WO 96US4189 960327
PRIORITY (CC, No, Date): US 414971 950331; US 563673 951128
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED DIVISIONAL NUMBER(S) - PN (AN):
EP 1329226 (EP 2003008324)
INTERNATIONAL PATENT CLASS: A61K-047/48; A61P-025/36
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200348	271
CLAIMS B	(German)	200348	259
CLAIMS B	(French)	200348	313
SPEC B	(English)	200348	21208
Total word count - document A			0
Total word count - document B			22051
Total word count - documents A + B			22051

13/3,AB/7 (Item 7 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00742082
Production in bacteria and yeast of hemoglobin and analogues thereof in non-erythrocyte cells
Herstellung von Hamoglobin und Analogen davon in Nicht-Erythrozytzellen
Production d'hemoglobine et de ses analogues par des cellules non-erythrocytes
PATENT ASSIGNEE:
Baxter Biotech Technology S.a.r.l., (2587073), Route de Pierre-a-Bot 11, 2000 Neuchatel, (CH), (Proprietor designated states: all)
INVENTOR:
Hoffmann, Stephen J., 2090 Albion, Denver, Colorado 80207, (US)
Looker, Douglas L., 5567 S. Ouray Street, Aurora, Colorado 80015, (US)
Rosendal, Mary S., 3246 W. 11th Ave., Ct., Broomfield, Colorado 80020, (US)
Stetler, Gary L., 36 South Hudson, Denver, Colorado 80222, (US)
Wagenbach, Michael, 1645 Pine No. 4, Boulder, Colorado 80302, (US)
LEGAL REPRESENTATIVE:
Bassett, Richard Simon (52833), Eric Potter Clarkson, Park View House, 58 The Ropewalk, Nottingham NG1 5DD, (GB)
PATENT (CC, No, Kind, Date): EP 700997 A1 960313 (Basic)
EP 700997 B1 030730
APPLICATION (CC, No, Date): EP 95110064 900510;
PRIORITY (CC, No, Date): US 349623 890510; US 374161 890630; US 379116 890713
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 402300 (EP 90610036)
RELATED DIVISIONAL NUMBER(S) - PN (AN):
(EP 2003077231)
INTERNATIONAL PATENT CLASS: C12N-015/12; C07K-014/805; G01N-033/72; C12P-021/02

ABSTRACT EP 700997 A1
A method of producing a hemoglobin-like protein wherein an alpha globin-like polypeptide and a beta globin-like polypeptide are each expressed in transformed non-erythrocyte cells such as bacterial or yeast cells, the method comprising expressing the alpha and beta globin-like polypeptide in the same cell in such manner that the alpha and beta globin-like polypeptides are assembled and combined with heme so as to intracellularly produce a biologically functional hemoglobin-like protein in soluble, recoverable form. (see image in original document)

ABSTRACT WORD COUNT: 95
NOTE:
Figure number on first page: 9

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPAB96	449
CLAIMS B	(English)	200331	463
CLAIMS B	(German)	200331	479
CLAIMS B	(French)	200331	558
SPEC A	(English)	EPAB96	34889
SPEC B	(English)	200331	34360
Total word count - document A			35343
Total word count - document B			35860
Total word count - documents A + B			71203

13/3,AB/8 (Item 8 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00404389
Production of bacteria and yeast of hemoglobin and analogues thereof
Herstellung von Hamoglobin und Analogen davon durch Bakterien oder Hefen
Production d'hemoglobine et de ses analogues par des bacteries ou des levures
PATENT ASSIGNEE:
Somatogen Inc., (1610614), 2545 Central Avenue, Suite FD-1, Boulder, Colorado 80301, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
MEDICAL RESEARCH COUNCIL, (791450), 20 Park Crescent, London W1N 4AL, (GB), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Hoffman, Stephen J., 2090 Albion, Denver, CO 80207, (US)
Looker, Douglas L., 5567 S. Ouray Street, Aurora, CO 80015, (US)
Rosendal, Mary S., 3246 W. 11th Ave., Ct., Broomfield, CO 80020, (US)
Stetler, Gary L., 36 South Hudson, Denver, CO 80222, (US)
Wagenbach, Michael, 1645 Pine No.4, Boulder, CO 80302, (US)
Nagai, Kiyoshi, 100 Mowbray Road, Cambridge CB1 4TG, (GB)
LEGAL REPRESENTATIVE:
Plougmann, Ole et al (61271), c/o Plougmann & Vingtoft A/S, Sankt Annae Plads 11, P.O. Box 3007, 1021 Copenhagen K, (DK)
PATENT (CC, No, Kind, Date): EP 402300 A2 901212 (Basic)
EP 402300 A3 910130
EP 402300 B1 960911
APPLICATION (CC, No, Date): EP 90610036 900510;
PRIORITY (CC, No, Date): US 349623 890510; US 374161 890630; US 379116 890713
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/12; C12P-021/02; C07K-001/00; G01N-033/72;

ABSTRACT EP 402300 A2
Alpha subunits of hemoglobin are provided as a novel recombinant

di-alpha globin polypeptide comprising the two alpha subunits connected directly via peptide **bond** or indirectly by a flexible amino-acid or peptide **linker**. Di-alpha globin may be combined in vivo or in vitro with beta globin and heme to form hemoglobin. Tetrameric human hemoglobin and di-alpha/beta(sub 2) hemoglobin are produced in S. cerevisiae by three types of expression vectors:

1) two separate plasmids containing respectively alpha and beta globin genes expressed in diploid strains.
2) a single plasmid comprising alpha and beta globin genes expressed in either haploid or diploid strains.
3) a single plasmid containing di-alpha and beta globin genes expressed in haploid strains.

Tetrameric form or separate subunits can be recovered from the soluble fraction. So, 3 types of hemoglobin-like molecules can be produced: di-alpha/two beta, di-beta/two alpha or di-alpha/di-beta, with a long half life.

ABSTRACT WORD COUNT: 152

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	1338
CLAIMS B	(English)	EPAB96	1979
CLAIMS B	(German)	EPAB96	1818
CLAIMS B	(French)	EPAB96	2344
SPEC A	(English)	EPABF1	35130
SPEC B	(English)	EPAB96	34964
Total word count - document A			36471
Total word count - document B			41105
Total word count - documents A + B			77576

13/3,AB/9 (Item 9 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00233369
ORAL VACCINES
ORALE IMPFSTOFFE
VACCINS ORAUX
PATENT ASSIGNEE:
BIOTECHNOLOGY AUSTRALIA PTY. LTD., (374170), 28 Barcoo Street, East Roseville, NSW 2069, (AU), (Proprietor designated states: all)
INVENTOR:
RUSSELL-JONES, Gregory, John, 101/2 Artarmon Road, Willoughby, NSW 2068, (AU)
DE AIZPURUA, Henry, James, 9 Douglas Street, Bexley, NSW 2207, (AU)
HOWE, Peter, 6 Mundon Place, West Pennant Hills, NSW 2120, (AU)
RAND, Keith, Norman, 10A Ferncourt Avenue, Chatswood, NSW 2067, (AU)
LEGAL REPRESENTATIVE:
Adkins, Michael et al (42842), Withers & Rogers, Goldings House, 2 Hays Lane, London SE1 2HW, (GB)
PATENT (CC, No, Kind, Date): EP 222835 A1 870527 (Basic)
EP 222835 A1 880323
EP 222835 B1 940928

EP 222835 B2 000419
WO 8606635 861120
APPLICATION (CC, No, Date): EP 86903134 860514; WO 86AU135 860514
PRIORITY (CC, No, Date): AU 85566 850515; AU 853104 851025
DESIGNATED STATES: BE; CH; DE; FR; GB; IT; LI; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/385; C07K-017/00; C12N-001/20; C12N-015/00
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200016	1870
CLAIMS B	(German)	200016	1774
CLAIMS B	(French)	200016	2210
SPEC B	(English)	200016	8788
Total word count - document A			0
Total word count - document B			14642
Total word count - documents A + B			14642

Set	Items	Description
S14	52	S10/TI,DE,MAJ
S15	49	S14 NOT S12

>>>No matching display code(s) found in file(s): 65, 113

15/3,AB/1 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

06594216 References: 52
TITLE: COMPARATIVE IMMUNOGENICITY OF **CONJUGATES** COMPOSED OF ESCHERICHIA COLI O111 O-SPECIFIC POLYSACCHARIDE, PREPARED BY TREATMENT WITH ACETIC ACID OR HYDRAZINE, **BOUND** TO TETANUS **TOXOID** BY TWO SYNTHETIC SCHEMES
AUTHOR(S): GUPTA RK; EGAN W; BRYLA DA; ROBBINS JB; SZU SC (Reprint)
CORPORATE SOURCE: NICHHD/BETHESDA//MD/20892 (Reprint); NICHHD/BETHESDA//MD/20892; US FDA,CTR BIOL EVALUAT & RES/BETHESDA//MD/20892
PUBLICATION: INFECTION AND IMMUNITY, 1995, V63, N8 (AUG), P2805-2810
GENUINE ARTICLE#: RK640
ISSN: 0019-9567
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: Escherichia coli O111, of various H types and virulence factors, causes enteritis throughout the world, especially in young children. This O type is found rarely in healthy individuals. Serum antibodies to the O-specific polysaccharide of O111 lipopolysaccharide (LPS) protect mice and dogs against infection with this E. coli serotype. The O111 O-specific polysaccharide is composed of a pentasaccharide repeat unit with two colitoses bound to the C-3 and C-6 of glucose in a trisaccharide backbone; this structure is identical to that of Salmonella adelaide (O35), another enteric pathogen. Nonpyrogenic O111 O-specific polysaccharide was prepared by treatment of its LPS with acetic acid (O-SP) or the organic base hydrazine (DeA-LPS). The O-SP had a reduced concentration of colitose. These products were derivatized with adipic acid dihydrazide (ADH) or

thiolated with N-succinimidyl-3(2-pyridyldithio) propionate (SPDP). The four derivatives were covalently bound to tetanus toroid (TT) by carbodiimide-mediated condensation or with SPDP to form conjugates. Immunization of BALB/c and general-purpose mice by a clinically acceptable route showed that DeA-LPST-TTADH, of the four conjugates, elicited the highest level of LPS antibodies. Possible reasons to explain this differential immunogenicity between the four conjugates are discussed.

15/3,AB/2 (Item 2 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

06319801 References: 24
TITLE: SYNTHESIS AND CHARACTERIZATION OF A POLYVALENT ESCHERICHIA COLI O-POLYSACCHARIDE **TOXIN** A **CONJUGATE** VACCINE
AUTHOR(S): CRYZ SJ; QUE JO; CROSS AS; FURER E
CORPORATE SOURCE: SWISS SERUM & VACCINE INST,POB 2707/CH-3001 BERN//SWITZERLAND/ (Reprint); WALTER REED ARMY MED CTR,WALTER REED ARMY INST RES/WASHINGTON//DC/20307
PUBLICATION: VACCINE, 1995, V13, N5 (APR), P449-453
GENUINE ARTICLE#: QR844
ISSN: 0264-410X
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: A 12-valent Escherichia coli O-polysaccharide (O-PS)-toxin A conjugate vaccine was formulated Nonpyrogenic, low-molecular-weight O-PS, was derived from lipopolysaccharides (LPS) of the following serotypes: 01, 02, 04, 06, 07, 08, 012 015, 016, 018, 025, and 075. Individual O-PS were covalently coupled to Pseudomonas aeruginosa toxin A using adipic acid dihydrazide as a spacer molecule and carbodiimide as a coupling agent. On a weight basis, the final multivalent vaccine was composed of 43% O-PS and 57% toxin A. The vaccine was nontoxic and nonpyrogenic in standard animal tests. Immunization of rabbits engendered a marked rise (6-74-fold) in anti-LPS immunoglobulin G (IgG) antibody titers. When passively transferred to mice, immune turze rabbit IgG conferred statistically significant ($p<0.05$) protection against a challenge with 9 of the 12 vaccine serotypes. For two serotypes, although the mortality rate declined by greater than or equal to 50% in the passively immunized versus the control group, the difference did not reach statistical significance. The degree of protection provided by passively transferred IgG was influenced by both the anti-LPS antibody levels in the IgG preparation and the virulence of the challenge strain. Active immunization of mice with either conjugate vaccine or killed E. coli, whole cells did not confer protection. This was most probably due to the fact that these antigens induced a meagre anti-LPS IgG antibody response.

15/3,AB/3 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01726384
Antibody fragment-polymer **conjugates** and humanized anti-IL-8 monoclonal antibodies
Antikorperfragment-Polymarkonjugate und humanisierte monoklonale Antikorper

gegen IL-8
Conjugues de fragments d'anticorps et des polymeres et des anticorps monoclonaux humanises contre l'IL-8
PATENT ASSIGNEE:
Genentech, Inc., (4538310), Legal Department, 1 DNA Way, South San Francisco, CA 94080-4990, (US), (Applicant designated States: all)
INVENTOR:
Hsei, Vanessa, 5047 Capistrano Avenue, San Jose, CA 95129, (US)
Koumenis, Iphigenia, Apartment 6, 3820 Park Boulevard, Palo Alto, CA 94306, (US)
Leong, Steven R., 1914 Eldorado Avenue, Berkeley, CA 94707, (US)
Presta, Leonard R., 1900 Gough Street, No. 206, San Franisco, CA 94109, (US)
Shahrokh, Zahra, 24 Sotelo Avenue, San Franisco, CA 94116, (US)
Zapata, Gerardo A., 785 Widgeon Street, Foster City, CA 94404, (US)
LEGAL REPRESENTATIVE:
Kiddle, Simon John et al (79861), Mewburn Ellis, York House, 23 Kingsway, London WC2B 6HP, (GB)
PATENT (CC, No, Kind, Date): EP 1415998 A2 040506 (Basic)
APPLICATION (CC, No, Date): EP 2003019832 980220;
PRIORITY (CC, No, Date): US 804444 970221; US 12116 980122
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
RELATED PARENT NUMBER(S) - PN (AN):
EP 968291 (EP 98911392)
INTERNATIONAL PATENT CLASS: C07K-016/24; A61K-047/48; C12N-015/13; C12N-015/63; C12N-005/10; A61K-039/395; A61P-037/00

ABSTRACT EP 1415998 A2
Humanized anti-IL-8 monoclonal antibodies and variants thereof are described for use in diagnostic applications and in the treatment of inflammatory disorders. Also described is a conjugate formed by an antibody fragment covalently attached to a non-proteinaceous polymer, wherein the apparent size of the conjugate is at least about 500 kD. The conjugate exhibits substantially improved half-life, mean residence time, and/or clearance rate in circulation as compared to the underivatized parental antibody fragment.
ABSTRACT WORD COUNT: 73
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200419	1138
SPEC A	(English)	200419	69371
Total word count - document A			70509
Total word count - document B			0
Total word count - documents A + B			70509

15/3,AB/4 (Item 2 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01634685
Conjugates for treating inflammatory disorders and associated tissue damage
Konjugate zur Behandlung von Entzundungskrankheiten und von assozierter Gewebeschadigung
Conjugues pour le traitement des maladies inflammatoires et des lesions tissulaires associees
PATENT ASSIGNEE:
Osprey Pharmaceuticals Limited, (2943070), 3400 Petro-Canada Centre, 150-6th Avenue SW, Calgary, Alberta T2P 3Y7, (CA), (Applicant designated States: all)
INVENTOR:
McDonald, John R., 303 Victoria Drive, Baie D Urfe,Quebec H9X2J3, (CA)
Coggins, Philip J., 59 Winston Circle, Pointe Claire, Quebec H9S 4X5, (CA)
LEGAL REPRESENTATIVE:
Baldock, Sharon Claire et al (73341), BOULT WADE TENNANT, Verulam Gardens 70 Gray's Inn Road, London WC1X 8BT, (GB)
PATENT (CC, No, Kind, Date): EP 1346731 A1 030924 (Basic)
APPLICATION (CC, No, Date): EP 2003076150 990721;
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
RELATED PARENT NUMBER(S) - PN (AN):
EP 1098664 (EP 99932572)
INTERNATIONAL PATENT CLASS: A61K-047/48; A61K-048/00; C12N-015/19; C12N-015/62; C12N-015/29; C12N-015/31; C07K-014/52; C07K-019/00; C07K-014/415

ABSTRACT EP 1346731 A1
The present invention provides a conjugate, comprising a targeted agent comprising a cytotoxic agent or a nucleic acid encoding a cytotoxic agent and a chemokine receptor targeting agent selected from a chemokine or a portion thereof, wherein the conjugate binds to a chemokine receptor resulting in internalization of the linked targeted agent in cells bearing the receptor, wherein the chemokine receptor targeting agent specifically binds to chemokine receptors on immune effector cells.
ABSTRACT WORD COUNT: 73
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200339	1280
SPEC A	(English)	200339	44723
Total word count - document A			46003
Total word count - document B			0
Total word count - documents A + B			46003

15/3,AB/5 (Item 3 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01634597

Pretargeting methods and novel pretargeting **conjugates**
Pretargeting Verfahren und neue Konjugate zum Pretargeting
Procedes de preciblage et nouveaux conjugues pour le preciblage

PATENT ASSIGNEE:
NEORX CORPORATION, (727931), 410 West Harrison Street, Seattle Washington 98119, (US), (Applicant designated States: all)
INVENTOR:
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Mallet, Robert W., 14216 61st Avenue SE, Everett, WA 98208, (US)
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Axworthy, Donald B., 3615 27th Street, S.W., Brier, WA 98036, (US)
Gustavson, Linda M., 19809 31st Street, N.E., Seattle, WA 98155, (US)
LEGAL REPRESENTATIVE:
Jones, Helen Marjorie Meredith (57931), Gill Jennings & Every, Broadgate House, 7 Eldon Street, London EC2M 7LH, (GB)
PATENT (CC, No, Kind, Date): EP 1346730 A1 030924 (Basic)
APPLICATION (CC, No, Date): EP 2003008765 941207;
PRIORITY (CC, No, Date): US 163188 931207
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 733066 (EP 95905334)
INTERNATIONAL PATENT CLASS: A61K-047/48; A61P-007/02

ABSTRACT EP 1346730 A1
In one aspect the invention includes an "antibody cocktail" approach to multi-step targeting of an active agent to a target site. This comprises administering multiple targeting moiety conjugates, wherein the targeting moieties are antibodies with nonoverlapping patterns of cross-reactivity for epitopes at the target site and wherein each targeting conjugate has a ligand or anti-ligand that is complementary to a corresponding anti-ligand or ligand on the active agent conjugate. In a further aspect the invention includes a multi-step method for targeting specifically a thrombolytic agent to the site of a thrombus, wherein the targeting moiety may be an annexin. In another aspect annexin may be the targeting moiety in a multi-step method for delivery of an active agent to a site having exposed anionic membrane lipids. In a final aspect, the invention includes specifically the compound biotinamido-N-methylglycyl-seryl-O-succinamido-benzyl DOTA, a chelating structure which may be used to deliver radiometals to a target site.
ABSTRACT WORD COUNT: 153
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200339	650
SPEC A	(English)	200339	49185
Total word count - document A			49835
Total word count - document B			0
Total word count - documents A + B			49835

15/3,AB/6 (Item 4 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01621025
Immune responses against HPV **antigens** elicited by compositions comprising an HPV **antigen** and a stress protein or an expression vector capable of expression of these proteins
Immunresponse gegen HPV **Antigene** erregt von Zusammensetzungen die ein HPV **Antigen** und ein Stressprotein enthalten oder einen Expressionsvektor fahig zur Expression dieser Proteine
Reponses immunologiques contre des **antigenes** de HPV eveillees par des compositions contenant un **antigene** de HPV et une proteine de stress ou un vecteur d'expression capable d'exprimer cettes proteines
PATENT ASSIGNEE:
Stressgen Biotechnologies Corporation, (2563520), No. 120-4243 Glanford Avenue, Victoria, British Columbia V8Z 4B9, (CA), (Applicant designated States: all)
INVENTOR:
Chu, Randall, 2225 Windsor Road, Victoria, British Columbia V8S 3C8, (CA)
LEGAL REPRESENTATIVE:
VOSSIUS & PARTNER (100314), Siebertstrasse 4, 81675 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1336621 A2 030820 (Basic)
EP 1336621 A3 040317
APPLICATION (CC, No, Date): EP 2003001726 980320;
PRIORITY (CC, No, Date): US 54835 P 970805
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 1002110 (EP 98910557)
INTERNATIONAL PATENT CLASS: C07K-019/00; C12N-015/62; C12N-015/861; C12N-015/867; A61K-039/12; A61K-048/00; A61P-031/20; C07K-014/025

ABSTRACT EP 1336621 A2
The present invention relates to compositions for inducing an immune response, preferably a cellular, in particular a cell-mediated, cytolytic immune response, to human papillomavirus (HPV) protein antigens displayed by HPV or exhibited by infected cells including cells from cervical and other tumors. In one embodiment, compositions comprise an HPV protein antigen joined to a stress protein (or heat shock protein (Hsp)). The HPV protein antigen may be joined to the stress protein by chemical conjugation or noncovalently using linking moieties, or the HPV protein antigen and the stress protein may be joined in a fusion protein containing both HPV protein antigen and stress protein sequences. In another embodiment, compositions comprise an expression vector including, in expressible form, sequences encoding the HPV protein antigen and sequences encoding the stress protein. The expression vector can be introduced into cells of a subject, or it can be used to transduce cells of the subject ex vivo, resulting in the expression of an HPV protein antigen-stress protein fusion protein that will stimulate the subject's immune response to the HPV protein antigen. The present invention also relates to compositions comprising a stress protein linked to an HPV antigen and another pharmacologically acceptable component, to stress protein-HPV protein antigen fusions and conjugates and to expression vectors encoding and capable of directing the expression in a subject's cells of a fusion protein comprising a stress protein and an HPV protein

antigen sequence. The present invention also relates to uses of these compositions to induce immune responses against HPV and HPV protein antigen-exhibiting cells including HPV-associated tumors.
ABSTRACT WORD COUNT: 260
NOTE:
Figure number on first page: 1

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200334	648
SPEC A	(English)	200334	14504
Total word count - document A			15152
Total word count - document B			0
Total word count - documents A + B			15152

15/3,AB/7 (Item 5 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01543168
Human antibodies that **bind** human TNFalpha
Humane antikorper welche an humanen tnfalpha binden
Anticorps humains se fixant au facteur necrosant des tumeurs de type alpha
PATENT ASSIGNEE:
BASF AKTIENGESELLSCHAFT, (200001), , 67056 Ludwigshafen, (DE), (Applicant designated States: all)
INVENTOR:
Salfeld, Jochen G., 177 Old Westboro Road, North Grafton, Massachusetts 01536, (US)
Allen, Deborah J., 143a Shelbourne Road, London, N17 9YD, (GB)
Hoogenboom, Hendricus R.J.M., Muggenstraat 45 Bus 12, 3500 Hasselt, (BE)
Kaymakcalan, Zehra, Piccadilly Way, Westboro, Massachusetts 01581, (US)
Labkovsky, Boris, 1630 Worcester Road, Apartment 532, Framingham, Massachusetts 01701, (US)
Mankovich, John A., 416 Lowell Street, Andover, Massachusetts 01810, (US)
McGuinness, Brian T., 22 The Lane, Hauxton, Cambridge CB2 5HP, (GB)
Roberts, Andrew J., 15 Cavendish Road, Cambridge CB1 3AE, (GB)
Sakorafas, Paul, 6114 Arbor Drive, Shrewsbury, Massachusetts 01545, (US)
Schoenhaut, David, 55 East Ninth Street, Clifton, New Jersey 07011, (US)
Vaughan, Tristan J., 9 Villa Road, Impington, Cambridge CB4 4NZ, (GB)
White, Michael, 30 Angelica Drive, Framingham, Massachusetts 01701, (US)
Wilton, Alison J., 46 Huntingdon Road, Cambridge, CB3 0HH, (GB)
LEGAL REPRESENTATIVE:
Schweiger, Georg, Dr. et al (76743), Patentanwalte Reitstotter, Kinzebach & Partner Sternwartstrasse 4, 81679 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1285930 A2 030226 (Basic)
APPLICATION (CC, No, Date): EP 2002022788 970210;
PRIORITY (CC, No, Date): US 599226 960209; US 31476 P 961125
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 929578 (EP 97906572)
INTERNATIONAL PATENT CLASS: C07K-016/24; C12N-015/09; A61K-039/395

ABSTRACT EP 1285930 A2
Human antibodies, preferably recombinant human antibodies, that specifically bind to human tumor necrosis factor (alpha) (hTNF(alpha)) are disclosed. These antibodies have high affinity for hTNF(alpha) (e.g., Kd)) = 10-8) M or less), a slow off rate for hTNF(alpha) dissociation (e.g., Koff)) = 10-3) sec-1) or less) and neutralize hTNF(alpha) activity in vitro and in vivo. An antibody of the invention can be a full-length antibody or an antigen-binding portion thereof. The antibodies, or antibody portions, of the invention are useful for detecting hTNF(alpha) and for inhibiting hTNF(alpha) activity, e.g., in a human subject suffering from a disorder in which hTNF(alpha) activity is detrimental. Nucleic acids, vectors and host cells for expressing the recombinant human antibodies of the invention, and methods of synthesizing the recombinant human antibodies, are also encompassed by the invention.
ABSTRACT WORD COUNT: 133
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200309	3243
SPEC A	(English)	200309	21439
Total word count - document A			24682
Total word count - document B			0
Total word count - documents A + B			24682

15/3,AB/8 (Item 6 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01450687
Human A33 **antigen**-like protein and nucleic acids encoding it
Menschliches A33-**Antigen** -ahnliches Protein und dafur kodierende Nukleinsaure
Proteine semblable a l'**antigene** A33 humaine et acides nucleiques le codant
PATENT ASSIGNEE:
Genentech, Inc., (210486), 1 DNA Way, South San Francisco, CA 94080-4990, (US), (Applicant designated States: all)
INVENTOR:
Wood, William I., 35 South Down Court, Hillsborough, CA 94010, (US)
Goddard, Audrey, 110 Congo Street, San Francisco, CA 94131, (US)
Gurney, Austin, 1 Debbie Lane, Belmont, CA 94002, (US)
Yuan, Jean, 176 West 37th Avenue, San Mateo, CA 94403, (US)
Baker, Kevin P., 14006 Indian Run Drive, Darnestown, Maryland 20878, (US)
Chen, Jian, 121 York Drive, Princeton, New Jersey, 08540, (US)
LEGAL REPRESENTATIVE:
Denison, Christopher Marcus et al (94571), Mewburn Ellis York House 23 Kingsway, London WC2B 6HP, (GB)
PATENT (CC, No, Kind, Date): EP 1241180 A2 020918 (Basic)
EP 1241180 A3 030319
APPLICATION (CC, No, Date): EP 2002012900 990308;
PRIORITY (CC, No, Date): US 78936 980320
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI;

LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
RELATED PARENT NUMBER(S) - PN (AN):
(EP 99912321)
INTERNATIONAL PATENT CLASS: C07K-014/47; C07K-016/18; C12N-015/12; C12N-015/62

ABSTRACT EP 1241180 A2
The present invention is directed to novel polypeptides and to nucleic acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.
ABSTRACT WORD COUNT: 66
NOTE:
Figure number on first page: NONE
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200238	379
SPEC A	(English)	200238	26205
Total word count - document A			26584
Total word count - document B			0
Total word count - documents A + B			26584

15/3,AB/9 (Item 7 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01440200
Non-A, non-B hepatitis virus **antigen**, diagnostic methods and vaccines
Nicht-A, nicht-B Hepatitis Virus **Antigen**, diagnostische Verfahren und Impfstoffe
Antigene du virus de l'hepatite non-A, non B, procede diagnostique et vaccins
PATENT ASSIGNEE:
Helting, Torsten B., (3943100), P.O.Box 880963, San Francisco California 94188, (US), (Applicant designated States: all)
New York Blood Center, Inc., (228440), 310 East 67 Street, New York, New [redacted]
INVENTOR:
Zebedee, Suzanne, 2918 Avenida Valera, Carlsbad, CA 92009-7113, (US)
Inchauspe, Genevieve, Inserm Unite 271, 151 Cours Albert Thomas, 69424 Lyon Cedex 03, (FR)
Nasoff, Marc S., 11734 Mira Lago Way, San Diego, CA 92131-2386, (US)
Prince, Alfred M., 349 Stone Hill Road, Pound Ridge, NY 10576-0154, (US)
LEGAL REPRESENTATIVE:
VOSSIUS & PARTNER (100314), Siebertstrasse 4, 81675 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1227323 A1 020731 (Basic)
APPLICATION (CC, No, Date): EP 2002006640 910823;
PRIORITY (CC, No, Date): US 573643 900825; US 616369 901121; US 748564 910821
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE

RELATED PARENT NUMBER(S) - PN (AN):
EP 544838 (EP 91920080)
INTERNATIONAL PATENT CLASS: G01N-033/576; A61K-039/29

ABSTRACT EP 1227323 A1
The present invention relates to a DNA segment encoding a recombinant non-A, non-B hepatitis structural protein or fusion protein and a recombinant DNA (rDNA) molecule capable of expressing either protein. Cells transformed with the rDNA, methods for producing the proteins in addition to compositions containing the proteins, and their use in diagnostic methods and systems, and in vaccines are also described.
ABSTRACT WORD COUNT: 62
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200231	508
SPEC A	(English)	200231	27307
Total word count - document A			27815
Total word count - document B			0
Total word count - documents A + B			27815

15/3,AB/10 (Item 8 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01435420
Cellular and serum protein anchors and **conjugates**
Zell- und Serum-Proteinanker und Konjugate
Proteine serique et cellulaire d'ancrage et conjugues
PATENT ASSIGNEE:
Conjuchem, Inc., (1943478), 225 President-Kennedy, Bureau 3950, Montreal, Quebec H2X 3Y8, (CA), (Applicant designated States: all)
INVENTOR:
Pouletty, Phillipe, 3 O'Dell Place, Atherton, California 94027, (US)
Pouletty, Phillipe, 3 O'Dell Place, Atherton, California 94027, (US)
LEGAL REPRESENTATIVE:
Sutcliffe, Nicholas Robert et al (98861), Mewburn Ellis, York House, 23 Kingsway, London WC2B 6HP, (GB)
PATENT (CC, No, Kind, Date): EP 1216714 A1 020626 (Basic)
APPLICATION (CC, No, Date): EP 2001129699 940916;
PRIORITY (CC, No, Date): US 137821 931015; US 237346 940503
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 793506 (EP 94930447)
INTERNATIONAL PATENT CLASS: A61K-047/48

ABSTRACT EP 1216714 A1
Novel bifunctional reagents useful in providing extended in vivo lifetimes of physiologically active agents are provided. The reagents comprise conjugates of a first binding member specific for a target in a mammalian host, such as a toxin, drug of abuse, microbe, autoreactive

immune cell, infected or tumourous cell, antigen presenting cell, or the like, joined to a second binding member specific for a long-lived blood component, including cells, such as an erythrocyte, platelet or endothelial cell, and plasma proteins. These conjugates find use by extending the lifetime and availability of the target binding member for coupling the target and the blood component and thereby reducing the concentration free target, modulating the volume of distribution of the target, targeting the target to sites of enhanced immune response, facilitating target clearance from the bloodstream, or extending the stimulation of an immunogen.
ABSTRACT WORD COUNT: 140

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200226	343
SPEC A	(English)	200226	12076
Total word count - document A			12419
Total word count - document B			0
Total word count - documents A + B			12419

15/3,AB/11 (Item 9 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01406002
Heparin-**binding** growth factors for gene therapy and anterior eye disorders
Heparin-bindende Wachstumfaktoren zur Gentherapie und Behandlung von Augenerkrankungen im vorderen Bereich
Facteurs de croissance de fibroplastes pour la therapie genetique et le traitement de troubles du segment anterieur de l'oeil
PATENT ASSIGNEE:
PRIZM PHARMACEUTICALS, INC., (1745081), 11035 Roselle Street, San Diego, CA 92121-1204, (US), (Applicant designated States: all)
INVENTOR:
Sosnowski, Barbara A., 1013 Adella Avenue, Coronado, CA 92118, (US)
Houston, Lou L., 327 Pine Needles Drive, Del Mar, CA 92014, (US)
Baird, J. Andrew, 45 Linton Street, London N17 AN, (GB)
Nova, Michael P., 11025 North Torrey Pines Roaduit, Suite 200, La Jolla, CA 92037, (US)
LEGAL REPRESENTATIVE:
Gowshall, Jonathan Vallance et al (61531), FORRESTER & BOEHMERT Pettenkoferstrasse 20-22, 80336 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1188448 A2 020320 (Basic)
EP 1188448 A3 020417
APPLICATION (CC, No, Date): EP 2001125266 950315;
PRIORITY (CC, No, Date): US 213446 940315; US 213447 940315
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 776218 (EP 95916103)
INTERNATIONAL PATENT CLASS: A61K-047/48; A61K-048/00; A61K-041/00; C12N-015/62

ABSTRACT EP 1188448 A3

Preparations of conjugates of a heparin-binding growth factor and a targeted agent and compositions containing such preparations are provided. The conjugates contain a polypeptide that is reactive with an FGF receptor, such as bFGF, or another heparin-binding growth factor coupled to a targeted agent through a linker. The linker is selected to increase the specificity, toxicity, solubility, serum stability, and/or intracellular availability of the targeted moiety. Several linkers may be included in order to take advantage of desired properties of each linker. Pharmaceutical compositions containing these conjugates of FGF and a targeted agent and methods for prevention of recurrence of pterygii, closure of trabeculectomy and corneal hazing following excimer laser surgery are provided. The methods entail contacting the area of the eye that has been surgically treated with the composition during or immediately after surgery. Compositions of conjugates of a heparin-binding growth factor and a nucleic acid binding domain are provided. The conjugates bind nucleic acid molecules through the nucleic acid binding domain. These conjugates may be used to deliver nucleic acid encoding a cytotoxic protein or an antisense nucleic acid and the like to cells expressing receptors for the heparin-binding growth factor.

ABSTRACT WORD COUNT: 194

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200212	1732
SPEC A	(English)	200212	44443
Total word count - document A			46175
Total word count - document B			0
Total word count - documents A + B			46175

15/3,AB/12 (Item 10 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01326443
Cellular and serum protein anchors and **conjugates**
Zell- und Serum- proteinanker und Konjugate
Proteine serique et cellulaire d'ancrage et conjugues
PATENT ASSIGNEE:
ConjuChem, Inc., (1943475), 1801 de Maisonneuve Blvd, Suite 810, Montreal, Quebec, (CA), (Applicant designated States: all)
INVENTOR:
Pouletty, Philippe, 3 O'Dell Place, Atherton, CA 94027, (US)
Pouletty, Christine, 3 O'Dell Place, Atherton, CA 94027, (US)
LEGAL REPRESENTATIVE:
Walton, Sean Malcolm et al (77071), MEWBURN ELLIS, York House, 23 Kingsway, London WC2B 6HP, (GB)
PATENT (CC, No, Kind, Date): EP 1132097 A2 010912 (Basic)
EP 1132097 A8 011128
EP 1132097 A3 020206
APPLICATION (CC, No, Date): EP 2001107561 940916;
PRIORITY (CC, No, Date): US 137821 931015; US 237346 940503
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE

RELATED PARENT NUMBER(S) - PN (AN):
EP 793506 (EP 94930447)
INTERNATIONAL PATENT CLASS: A61K-047/48

ABSTRACT EP 1132097 A2
Novel bifunctional reagents useful in providing extended in vivo lifetimes of physiologically active agents are provided. The reagents comprise conjugates of a first binding member specific for a target in a mammalian host, such as a toxin, drug of abuse, microbe, autoreactive immune cell, infected or tumourous cell, antigen presenting cell, or the like, joined to a second binding member specific for a longlived blood component, including cells, such as an erythrocyte, platelet or endothelial cell, and plasma proteins. These conjugates find use by extending the lifetime and availability of the target binding member for coupling the target and the blood component and thereby reducing the concentration free target, modulating the volume of distribution of the target, targeting the target to sites of enhanced immune response, facilitating target clearance from the bloodstream, or extending the stimulation of an immunogen.
ABSTRACT WORD COUNT: 140

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200137	285
SPEC A	(English)	200137	12074
Total word count - document A			12359
Total word count - document B			0
Total word count - documents A + B			12359

15/3,AB/13 (Item 11 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01264843
Vaccines comprising a polysaccharide **antigen**-carrier protein **conjugate** and free carrier protein
Vakzine mit einem Polysaccharide **Antigen**-Tragerprotein Konjugat und freien Tragerprotein
Vaccins comprenant un conjugue **antigene** de polysaccharide-proteine porteuse et une proteine porteuse libre
PATENT ASSIGNEE:
SMITHKLINE BEECHAM BIOLOGICALS S.A., (1311860), 89 rue de l'Institut, 1330 Rixensart, (BE), (Applicant designated States: all)
INVENTOR:
Slaoui, Moncef Mohamed, SmithKline Beecham Biol.SA, rue de l'Institute 89 , 1330 Rixensart, (BE)
Hauser, Pierre, SmithKline Beecham Biologicals S.A, rue de l'Institute 89 , 1330 Rixensart, (BE)
LEGAL REPRESENTATIVE:
Privett, Kathryn Louise et al (81082), SmithKline Beecham plc, Corporate Intellectual Property, Two New Horizons Court - 2/NHC/1, Great West Road, Brentford, Middlesex TW8 9EP, (GB)
PATENT (CC, No, Kind, Date): EP 1090642 A2 010411 (Basic)
EP 1090642 A3 010822

APPLICATION (CC, No, Date): EP 2000203772 960604;
PRIORITY (CC, No, Date): US 472639 950607; GB 9512827 950623; GB 9513443 950701; GB 9525657 951215
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: SI
RELATED PARENT NUMBER(S) - PN (AN):
EP 831901 (EP 96920790)
INTERNATIONAL PATENT CLASS: A61K-039/385; A61K-039/116; A61K-039/295; A61K-039/00; A61P-031/00

ABSTRACT EP 1090642 A2
The present invention relates to combination vaccines comprising a conjugated polysaccharide antigen linked to a carrier protein, and wherein the carrier protein is also present as a free antigen in the vaccine composition, characterised in that the ratio of polysaccharide to protein is from 1:0:3 to 1:2. In particular the vaccine composition of the present invention relates to a multivalent vaccine, that is a vaccine for the amelioration or treatment of more than one disease states. The present invention also relates to the production and use of such a vaccine in medicine.
ABSTRACT WORD COUNT: 93

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200115	261
SPEC A	(English)	200115	2411
Total word count - document A			2672
Total word count - document B			0
Total word count - documents A + B			2672

15/3,AB/14 (Item 12 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01148679
Outer membrane proteins from actinobacillus pleuropneumoniae
Hauptproteine der Aussenmembran von actinobacillus pleuropneumoniae
Proteines principales de la membrane externe de actinobacillus pleuropneumoniae
PATENT ASSIGNEE:
Pfizer Products Inc., (2434221), Eastern Point Road, Groton, Connecticut 06340, (US), (Applicant designated States: all)
INVENTOR:
Ankenbauer, Robert Gerard, Pfizer Inc., Central Research Division, Eastern Point Road, Groton, Connecticut 06340, (US)
Baarsch, Mary Jo, Pfizer Inc., Central Research Division, Eastern Point Road, Groton, Connecticut 06340, (US)
Campos, Manuel, Pfizer Inc., Central Research Division, Eastern Point Road, Groton, Connecticut 06340, (US)
Keich, Robin Lee, Pfizer Inc., Central Research Division, Eastern Point Road, Groton, Connecticut 06340, (US)
Rosey, Everett Lee, Pfizer Inc., Central Research Division, Eastern Point

Road, Groton, Connecticut 06340, (US)
Warren-Stewart, Lynn Marie, Pfizer Inc., Central Research Division, Eastern Point Road, Groton, Connecticut 06340, (US)
Suiter, Brian Thomas, Pfizer Inc., Central Research Division, Eastern Point Road, Groton, Connecticut 06340, (US)
LEGAL REPRESENTATIVE:
Simpson, Alison Elizabeth Fraser et al (77401), Urquhart-Dykes & Lord, 30 Welbeck Street, London W1G 8ER, (GB)
PATENT (CC, No, Kind, Date): EP 1001025 A2 000517 (Basic)
EP 1001025 A3 020410
APPLICATION (CC, No, Date): EP 99308262 991020;
PRIORITY (CC, No, Date): US 105285 981022
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: C12N-015/12; C12N-015/62; C07K-014/285; A61K-039/07; G01N-033/68

ABSTRACT EP 1001025 A2
The present invention is directed to five novel, low molecular weight proteins from Actinobacillus pleuropneumoniae (APP), which are capable of inducing, or contributing to the induction of, a protective immune response in swine against APP. The present invention is further directed to polynucleotide molecules having nucleotide sequences that encode the proteins, as well as vaccines comprising the proteins or polynucleotide molecules, and methods of making and using the same.
ABSTRACT WORD COUNT: 70
NOTE:
Figure number on first page: 1

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200020	3435
SPEC A	(English)	200020	24943
Total word count - document A			28378
Total word count - document B			0
Total word count - documents A + B			28378

15/3,AB/15 (Item 13 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01132814
CONJUGATES FOR TREATING INFLAMMATORY DISORDERS AND ASSOCIATED TISSUE DAMAGE
KONJUGATE ZUR BEHANDLUNG VON ENTZUNDUNGSKRANKHEITEN UND VON ASSOZIERTER GEWEBESCHADIGUNG
TRAITEMENT DE DEGATS TISSULAIRES SECONDAIRES, ETATS INFLAMMATOIRES ET AUTRES TROUBLES, ET COMPOSITIONS A CET EFFET
PATENT ASSIGNEE:
Osprey Pharmaceuticals Limited, (2943070), 3400 Petro-Canada Centre, 150-6th Avenue SW, Calgary, Alberta T2P 3Y7, (CA), (Proprietor designated states: all)
INVENTOR:

MCDONALD, John, R., 60 Governor Drive SW, Calgary, Alberta T3E 4Y9, (CA)
COGGINS, Philip, J., 4211, 5A Street SW, Calgary, Alberta T2S 2G8, (CA)
LEGAL REPRESENTATIVE:
Baldock, Sharon Claire et al (73341), BOULT WADE TENNANT, Verulam Gardens 70 Gray's Inn Road, London WC1X 8BT, (GB)
PATENT (CC, No, Kind, Date): EP 1098664 A2 010516 (Basic)
EP 1098664 B1 030806
WO 2000004926 000203
APPLICATION (CC, No, Date): EP 99932572 990721; WO 99CA659 990721
PRIORITY (CC, No, Date): US 120523 980722
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
RELATED DIVISIONAL NUMBER(S) - PN (AN):
(EP 2003076150)
INTERNATIONAL PATENT CLASS: A61K-047/48; A61K-048/00; C12N-015/19; C12N-015/62; C12N-015/29; C12N-015/31; C07K-014/52; C07K-019/00; C07K-014/415; A61P-029/00
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200332	3371
CLAIMS B	(German)	200332	3083
CLAIMS B	(French)	200332	4220
SPEC B	(English)	200332	46019
Total word count - document A			0
Total word count - document B			56693
Total word count - documents A + B			56693

15/3,AB/16 (Item 14 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01029791
IMMUNE RESPONSES AGAINST HPV **ANTIGENS** ELICITED BY COMPOSITIONS COMPRISING AN HPV **ANTIGEN** AND A STRESS PROTEIN OR AN EXPRESSION VECTOR CAPABLE OF EXPRESSION OF THESE PROTEINS
IMMUNRESPONSE GEGEN HPV **ANTIGENE** ERREGT VON ZUSAMMENSETZUNGEN DIE EIN HPV **ANTIGEN** UND EIN STRESSPROTEIN ENTHALTEN ODER EINEN EXPRESSIONSVEKTOR FAHIG ZUR EXPRESSION DIESER PROTEINE
REPONSES IMMUNITAIRES CONTRE LES **ANTIGENES** DU VPH ET DECLENCHEES PAR DES COMPOSITIONS COMPRENANT UN **ANTIGENE** DU VPH, ET PROTEINE DU STRESS OU VECTEUR D'EXPRESSION CAPABLE D'EXPRIMER CES PROTEINES
PATENT ASSIGNEE:
Stressgen Biotechnologies Corporation, (2563520), No. 120-4243 Glanford Avenue, Victoria, British Columbia V8Z 4B9, (CA), (Proprietor designated states: all)
INVENTOR:
MIZZEN, Lee, 1936 Quamichan Street, Victoria, British Columbia V8S 2C4, (CA)
CHU, Randall, 2225 Windsor Road, Victoria, British Columbia V8S 3C8, (CA)
WU, Huacheng Bill, Dr., 403-1535, Jubilee Avenue, Victoria British Columbia - V8R 4N4, (CA)

LEGAL REPRESENTATIVE:
Barth, Renate et al (62532), Vossius & Partner Siebertstr. 4, 81675 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1002110 A1 000524 (Basic)
EP 1002110 B1 030129
WO 99007860 990218
APPLICATION (CC, No, Date): EP 98910557 980320; WO 98CA246 980320
PRIORITY (CC, No, Date): US 54835 P 970805
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED DIVISIONAL NUMBER(S) - PN (AN):
(EP 2003001726)
INTERNATIONAL PATENT CLASS: C12N-015/70; A61K-039/385; A61K-039/12; C07K-019/00; A61K-048/00
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200305	618
CLAIMS B	(German)	200305	551
CLAIMS B	(French)	200305	760
SPEC B	(English)	200305	14831
Total word count - document A			0
Total word count - document B			16760
Total word count - documents A + B			16760

15/3,AB/17 (Item 15 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00987210
ANTIBODY FRAGMENT-POLYMER **CONJUGATES**
ANTIKORPERFRAGMENT-POLYMERKONJUGATE
CONJUGUES DE POLYMERES ET DE FRAGMENTS D'ANTICORPS
PATENT ASSIGNEE:
Genentech, Inc., (210486), 1 DNA Way, South San Francisco, CA 94080-4990, (US), (Proprietor designated states: all)
INVENTOR:
HSEI, Vanessa, 5047 Capistrano Avenue, San Jose, CA 95129, (US)
KOUMENIS, Iphigenia, Apartment 6, 3820 Park Boulevard, Palo Alto, CA 94306, (US)
LEONG, Steven, R., 1914 Eldorado Avenue, Berkeley, CA 94707, (US)
PRESTA, Leonard, G., 1900 Gough Street 206, San Francisco, CA 94109, (US)
SHAHROKH, Zahra, 24 Sotelo Avenue, San Francisco, CA 94116, (US)
ZAPATA, Gerardo, A., 785 Widgeon Street, Foster City, CA 94404, (US)
LEGAL REPRESENTATIVE:
Kiddle, Simon John et al (79861), Mewburn Ellis, York House, 23 Kingsway, London WC2B 6HP, (GB)
PATENT (CC, No, Kind, Date): EP 968291 A2 000105 (Basic)
EP 968291 B1 040128
WO 1998037200 980827
APPLICATION (CC, No, Date): EP 98911392 980220; WO 98US3337 980220
PRIORITY (CC, No, Date): US 804444 970221; US 12116 980122

DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
RELATED DIVISIONAL NUMBER(S) - PN (AN):
(EP 2003019832)
INTERNATIONAL PATENT CLASS: C12N-015/13; C07K-019/00; A61K-047/48; C07K-016/24; C12N-015/85; C12N-005/10
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200405	1123
CLAIMS B	(German)	200405	1012
CLAIMS B	(French)	200405	1207
SPEC B	(English)	200405	47093
Total word count - document A			0
Total word count - document B			50435
Total word count - documents A + B			50435

15/3,AB/18 (Item 16 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00895368
CYTOMODULATING **CONJUGATES** OF MEMBERS OF SPECIFIC **BINDING** PAIRS
ZELLMODULIERENDE KONJUGATE AUS ELEMENTEN AUS SPEZIFISCHEN BINDUNGSPAAREN
CONJUGUES CYTOMODULANTS D'ELEMENTS DE PAIRES DE LIAISON SPECIFIQUES
PATENT ASSIGNEE:
SANGSTAT MEDICAL CORPORATION, (1227840), 1505B Adams Drive, Menlo Park, CA 94025, (US), (Proprietor designated states: all)
INVENTOR:
POULETTY, Philippe, 3 O'Dell Place, Atherton, CA 94027, (US)
LEGAL REPRESENTATIVE:
Baldock, Sharon Claire et al (73341), BOULT WADE TENNANT, Verulam Gardens 70 Gray's Inn Road, London WC1X 8BT, (GB)
PATENT (CC, No, Kind, Date): EP 833666 A2 980408 (Basic)
EP 833666 A3 980708
EP 833666 B1 031210
WO 97037690 971016
APPLICATION (CC, No, Date): EP 97917902 970409; WO 97US5842 970409
PRIORITY (CC, No, Date): US 630383 960410
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-047/48
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200350	529
CLAIMS B	(German)	200350	509
CLAIMS B	(French)	200350	580
SPEC B	(English)	200350	8778
Total word count - document A			0

Total word count - document B 10396
Total word count - documents A + B 10396

15/3,AB/19 (Item 17 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00880611
HUMAN ANTIBODIES THAT **BIND** HUMAN TNFalpha
HUMANE ANTIKORPER WELCHE AN HUMANEN TNFalpha BINDEN
ANTICORPS HUMAINS SE FIXANT AU FACTEUR NECROSANT DES TUMEURS DE TYPE alpha
PATENT ASSIGNEE:
BASF Aktiengesellschaft, (200000), Carl-Bosch-Strasse 38, 67063 Ludwigshafen, (DE), (Proprietor designated states: all)
INVENTOR:
SALFELD, Jochen, G., 177 Old Westboro Road, North Grafton, MA 01536, (US)
ALLEN, Deborah, J., 143a Shelbourne Road, London N17 9YD, (GB)
KAYMAKCALAN, Zehra, 4 Piccadilly Way, Westboro, MA 01581, (US)
LABKOVSKY, Boris, Apartment 532, 1630 Worcester Road, Framingham, MA 01701, (US)
MANKOVICH, John, A., 416 Lowell Street, Andover, MA 01810, (US)
MCGUINESS, Brian, T., 22 The Lane, Hauxton, Cambridge CB2 5HP, (GB)
ROBERTS, Andrew, J., 15 Cavendish Road, Cambridge CB1 3AE, (GB)
SAKORAFAS, Paul, 6114 Arbor Drive, Shrewsbury, MA 01545, (US)
HOOGENBOOM, Hendricus, R., J., M., Muggenstraat 45, Bus 12, B-3500 Hasselt, (BE)
SCHOENHAUT, David, 55 East Ninth Street, Clifton, NJ 07011, (US)
VAUGHAN, Tristan, J., 9 Villa Road, Impington, Cambridge CB4 4NZ, (GB)
WHITE, Michael, 30 Angelica Drive, Framingham, MA 01701, (US)
WILTON, Alison, J., 46 Huntingdon Road, Cambridge CB3 0HH, (GB)
LEGAL REPRESENTATIVE:
Riedl, Peter, Dr. et al (57561), Patentanwalte Reitstotter, Kinzebach & Partner Postfach 86 06 49, 81633 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 929578 A1 990721 (Basic)
EP 929578 B1 030502
WO 97029131 970814
APPLICATION (CC, No, Date): EP 97906572 970210; WO 97US2219 970210
PRIORITY (CC, No, Date): US 599226 960209; US 31476 P 961125
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED DIVISIONAL NUMBER(S) - PN (AN):
EP 1285930 (EP 2002022788)
INTERNATIONAL PATENT CLASS: C07K-016/24; C12N-015/13; C12N-015/64; C12N-005/10; C12N-001/21; A61K-039/395; G01N-033/68
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200318	2518
CLAIMS B	(German)	200318	2473
CLAIMS B	(French)	200318	2943
SPEC B	(English)	200318	22910

Total word count - document A 0
Total word count - document B 30844

Total word count - documents A + B 30844

15/3,AB/20 (Item 18 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00852220
Methods of improving allograft or xenograft tolerance by administration of an LFA-3 or CD2 **binding** protein
Verfahren zur Verbesserung der Toleranz fur Allotransplantaten und Xenotransplantaten durch Verabreichung eines LFA-3- oder CD2-Bindungsproteins
Procedes d'amelioration de la tolerance des greffes allogenes ou xenogenes par administration d'une proteine liante a LFA-3 ou CD2
PATENT ASSIGNEE:
BIOGEN, INC., (1049451), 14 Cambridge Center, Cambridge Massachusetts 02142, (US), (Proprietor designated states: all)
INVENTOR:
Wallner, Barbara, P./7 Centre Street, Cambridge, MA 02139, (US)
Benjamin, Christopher, D./2 Oak Hill Lane, Beverly, MA 01915, (US)
LEGAL REPRESENTATIVE:
Ruffles, Graham Keith (43041), MARKS & CLERK, 57-60 Lincoln's Inn Fields, London WC2A 3LS, (GB)
PATENT (CC, No, Kind, Date): EP 786255 A1 970730 (Basic)
EP 786255 B1 011212
APPLICATION (CC, No, Date): EP 96117245 921006;
PRIORITY (CC, No, Date): US 772705 911007; US 850706 920312
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 607353 (EP 92922682)
INTERNATIONAL PATENT CLASS: A61K-038/17

ABSTRACT EP 786255 A1
A protein that binds CD2, which is a derivative of a soluble LFA-3 polypeptide, the derivative being an immunoglobulin fusion comprising the soluble LFA-3 polypeptide fused to an immunoglobulin region, or being the soluble LFA-3 polypeptide linked to a pharmaceutical agent, is used in the preparation of a medicament for use in a method of improving tolerance of transplanted allograft tissue or xenograft tissue in a mammal, including a human, wherein the method comprises implanting in the mammal an allograft or a xenograft and administering the protein.
ABSTRACT WORD COUNT: 88
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	199707W5	270
CLAIMS B	(English)	200150	214
CLAIMS B	(German)	200150	203
CLAIMS B	(French)	200150	228
SPEC A	(English)	199707W5	10759
SPEC B	(English)	200150	9008

Total word count - document A 11030
Total word count - document B 9653
Total word count - documents A + B 20683

15/3,AB/21 (Item 19 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00829143
VACCINE COMPRISING A POLYSACCHARIDE **ANTIGEN**-CARRIER PROTEIN **CONJUGATE** AND FREE CARRIER PROTEIN
VAKZINE MIT EINEM POLYSACCHARIDE **ANTIGEN**-TRAGERPROTEIN KONJUGAT UND FREIEN TRAGERPROTEIN
VACCINS COMPRENANT UN CONJUGUE **ANTIGENE** DE POLYSACCHARIDE-PROTEINE PORTEUSE ET UNE PROTEINE PORTEUSE LIBRE
PATENT ASSIGNEE:
SMITHKLINE BEECHAM BIOLOGICALS S.A., (1311860), 89 rue de l'Institut, 1330 Rixensart, (BE), (Proprietor designated states: all)
INVENTOR:
SLAOUI, Moncef Mohamed, SmithKline Beecham Biologicals S.A., Rue de l'Institut 89 1330 Rixensart, (BE)
HAUSER, Pierre, SmithKline Beecham Biologicals S.A., Rue de l'Institut 89 1330 Rixensart, (BE)
LEGAL REPRESENTATIVE:
Dalton, Marcus Jonathan William et al (60102), SmithKline Beecham plc Corporate Intellectual Property, Two New Horizons Court, Brentford, Middlesex TW8 9EP, (GB)
PATENT (CC, No, Kind, Date): EP 831901 A1 980401 (Basic)
EP 831901 B1 010919
WO 9640242 961219
APPLICATION (CC, No, Date): EP 96920790 960604; WO 96EP2436 960604
PRIORITY (CC, No, Date): US 472639 950607; GB 9512827 950623; GB 9513443 950701; GB 9525657 951215
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: SI
RELATED DIVISIONAL NUMBER(S) - PN (AN):
EP 1090642 (EP 2000203772)
INTERNATIONAL PATENT CLASS: A61K-039/385; A61K-039/00; A61K-039/39
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200138	195
CLAIMS B	(German)	200138	179
CLAIMS B	(French)	200138	214
SPEC B	(English)	200138	2532

Total word count - document A 0
Total word count - document B 3120
Total word count - documents A + B 3120

15/3,AB/22 (Item 20 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00804486
Neisseria meningitidis capsular polysaccharide **conjugates**
Konjugate von Neisseria Meningitidis Kapselpolysacchariden
Composes conjugues a partir de polysaccharides capsulaires de Neisseria meningitidis

PATENT ASSIGNEE:
CONNAUGHT LABORATORIES LIMITED, (267451), 1755 Steeles Avenue West, Willowdale Ontario M2R 3T4, (CA), (applicant designated states: BE;DE;FR;GB;IT)
INVENTOR:
Kandil, Ali, 245 Park Home Avenue, Willowdale, Ontario M2R 1A1, (CA)
Klein, Michel H., 16 Munro Boulevard, Willowdale, Ontario M2P 1B9, (CA)
Chong, Pele, 32 Estoril Street, Richmond Hill, Ontario L4C 0E6, (CA)
LEGAL REPRESENTATIVE:
Smart, Peter John (43071), W.H. BECK, GREENER & CO 7 Stone Buildings Lincoln's Inn, London WC2A 3SZ, (GB)

PATENT (CC, No, Kind, Date): EP 747063 A2 961211 (Basic)
EP 747063 A3 990324
APPLICATION (CC, No, Date): EP 96304311 960607;
PRIORITY (CC, No, Date): US 474392 950607
DESIGNATED STATES: BE; DE; FR; GB; IT
INTERNATIONAL PATENT CLASS: A61K-047/48; A61K-039/095;

ABSTRACT EP 747063 A2
Capsular polysaccharides containing multiple sialic acid residues, particularly the Group B polysaccharide of Neisseria meningitidis, are modified by chemical reaction to randomly introduce pendant reactive residues of heterobifunctional linker molecules to the polysaccharide backbone. The capsular polysaccharide is deacetylated and the heterobifunctional linker molecule is reacted with the deacetylated material and any residual amino groups are blocked by reaction with alkyl acid anhydride. The introduction of the linker molecules to the polysaccharide chain between the termini enables the polysaccharide to be linked to a carrier molecule, such as a protein, to enhance the immunogenicity of the polysaccharide. The conjugate molecule may be formulated as an immunogenic composition for raising antibodies in a host to the polysaccharide.
ABSTRACT WORD COUNT: 138

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPAB96	718
SPEC A	(English)	EPAB96	6289
Total word count - document A			7007
Total word count - document B			0
Total word count - documents A + B			7007

15/3,AB/23 (Item 21 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00771468

PEPTIDE NUCLEIC ACID **CONJUGATES**
PEPTID-NUKLEINSAURE-KONJUGATE
CONJUGUES D'ACIDES NUCLEIQUES PEPTIDIQUES
PATENT ASSIGNEE:
ISIS PHARMACEUTICALS, INC., (1382620), 2280 Faraday Avenue, Carlsbad, CA 92008, (US), (Proprietor designated states: all)
BUCHARDT, Dorte, (1895570), Sondergardsvej 73, 3500 Vaerlose, (DK), (Proprietor designated states: all)
NIELSEN, Peter Eigil, (1584400), Hjortevanget 509, 2980 Kokkedal, (DK), (Proprietor designated states: all)
EGHOLM, Michael, (1584382), 1231 Lexington Ridge Drive, Lexington, Massachusetts 02173, (US), (Proprietor designated states: all)
INVENTOR:
NIELSEN, Peter, Hjortevanget 509, DK-2980 Kokkedal, (DK)
EGHOLM, Michael, 1231 Lexington Ridge Drive, Lexington, MA 02173, (US)
BUCHARDT, Ole +di, deceased, ., (DK)
SONNECHSEN, Soren, Holst, Gronhojgardsvej 13, DK-2630 Tastrup, (DK)
LOHSE, Jesper, Staerevej 52, 2.tv, DK-2400 Copenhagen N, (DK)
MANOHARAN, Muthiah, 7634 Reposado Drive, Carlsbad, CA 92009, (US)
KIELY, John, 4230 Corte Facil, San Diego, CA 92130, (US)
GRIFFITH, Michael, 3686 Carmel Landing, San Diego, CA 92130, (US)
SPRANKLE, Kelly, Apartment 61 920 Sycamore Avenue, Vista, CA 92083, (US)
LEGAL REPRESENTATIVE:
Hallybone, Huw George (53031), Carpmaels and Ransford, 43 Bloomsbury Square, London WC1A 2RA, (GB)
PATENT (CC, No, Kind, Date): EP 804456 A1 971105 (Basic)
EP 804456 A1 990519
EP 804456 B1 020821
WO 96011205 960418
APPLICATION (CC, No, Date): EP 95938726 951006; WO 95US12931 951006
PRIORITY (CC, No, Date): US 319411 941006
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C07K-014/00; A61K-047/48
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200234	1552
CLAIMS B	(German)	200234	1529
CLAIMS B	(French)	200234	1937
SPEC B	(English)	200234	40535
Total word count - document A			0
Total word count - document B			45553
Total word count - documents A + B			45553

15/3,AB/24 (Item 22 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00696795
CELLULAR AND SERUM PROTEIN ANCHORS AND **CONJUGATES**
ZELL- UND SERUM- PROTEINANKER UND KONJUGATE
PROTEINE SERIQUE ET CELLULAIRE D'ANCRAGE ET CONJUGUES

PATENT ASSIGNEE:
ConjuChem, Inc., (1943475), 1801 de Maisonneuve Blvd, Suite 810, Montreal, Quebec, (CA), (Proprietor designated states: all)
INVENTOR:
POULETTY, Philippe, 3 O'Dell Place, Atherton, CA 94027, (US)
POULETTY, Christine, 3 O'Dell Place, Atherton, CA 94027, (US)
LEGAL REPRESENTATIVE:
Walton, Sean Malcolm et al (77071), MEWBURN ELLIS, York House, 23 Kingsway, London WC2B 6HP, (GB)
PATENT (CC, No, Kind, Date): EP 793506 A1 970910 (Basic)
EP 793506 A1 981111
EP 793506 B1 020417
WO 9510302 950420
APPLICATION (CC, No, Date): EP 94930447 940916; WO 94US10547 940916
PRIORITY (CC, No, Date): US 137821 931015; US 237346 940503
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED DIVISIONAL NUMBER(S) - PN (AN):
EP 1132097 (EP 2001107561)
(EP 2001129699)
INTERNATIONAL PATENT CLASS: A61K-039/395; C07K-016/28; C07K-016/46; A61K-047/48; A61K-039/385
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200216	471
CLAIMS B	(German)	200216	432
CLAIMS B	(French)	200216	525
SPEC B	(English)	200216	9703
Total word count - document A			0
Total word count - document B			11131
Total word count - documents A + B			11131

15/3,AB/25 (Item 23 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00655070
POLYSACCHARIDE-PROTEIN **CONJUGATES**
KONJUGATE BESTEHEND AUS POLYSACCHARID UND PROTEIN
CONJUGUES DE POLYSACCHARIDE-PROTEINE
PATENT ASSIGNEE:
THE UNITED STATES OF AMERICA, as represented by the Secretary of the Department of Health and Human Services, (1861302), Office of Technology Transfert, 6011 Executive Blvd., Suite 325, Rockville, Maryland 20852, (US), (Proprietor designated states: all)
INVENTOR:
SCHNEERSON, Rachel, 10601 Weymouth Street, Bethesda, MD 20814, (US)
ROBBINS, John B., 3901 Rosemary Street, Chevy Chase, MD 20815, (US)
SARVAMANGALA, Devi J.N., 6224 Copper Sky Court, Columbia, MD 21405, (US)
LEGAL REPRESENTATIVE:
Perry, Robert Edward (41331), GILL JENNINGS & EVERY Broadgate House 7 Eldon Street, London EC2M 7LH, (GB)

PATENT (CC, No, Kind, Date): EP 630260 A1 941228 (Basic)
EP 630260 A1 950607
EP 630260 B1 010124
WO 9216232 921001
APPLICATION (CC, No, Date): EP 92908970 920312; WO 92US1796 920312
PRIORITY (CC, No, Date): US 667170 910312
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; MC; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/385; A61K-039/095; A61K-039/102; A61K-039/108; A61K-039/116; C07K-017/10; C07H-013/02
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200104	429
CLAIMS B	(German)	200104	374
CLAIMS B	(French)	200104	544
SPEC B	(English)	200104	5147
Total word count - document A			0
Total word count - document B			6494
Total word count - documents A + B			6494

15/3,AB/26 (Item 24 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00584588
ESCHERICHIA COLI O-POLYSACCHARIDE-PROTEIN **CONJUGATE** VACCINE
ESCHERICHIA COLI IMPFSTOFFE AUF DER BASIS VON O-POLYSACCHARID-PROTEIN KONJUGATEN
VACCIN A BASE DE CONJUGUES DE POLYSACCHARIDE-O D'ESCHERICHIA COLI ET D'UNE PROTEINE
PATENT ASSIGNEE:
CRYZ, Stanley J., (1618470), Stampachgrasse 6, CH-3065 Bolligen, (CH), (Proprietor designated states: all)
INVENTOR:
CRYZ, Stanley, J., Stampachgrasse 6, CH-3065 Bolligen, (US)
FURER, Emil, P., Pelikanweg 9, CH-3074 Muri, (CH)
LEGAL REPRESENTATIVE:
Grunecker, Kinkeldey, Stockmair & Schwanhausser Anwaltssozietat (100721), Maximilianstrasse 58, 80538 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 598818 A1 940601 (Basic)
EP 598818 A1 950405
EP 598818 B1 010131
WO 9303765 930304
APPLICATION (CC, No, Date): EP 92918016 920811; WO 92US6531 920811
PRIORITY (CC, No, Date): US 743787 910812
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/385; A61K-039/116; A61K-039/108; A61K-039/02; C07K-017/10; C07K-002/00; C07K-014/245
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200105	1528
CLAIMS B	(German)	200105	1453
CLAIMS B	(French)	200105	1654
SPEC B	(English)	200105	3891
Total word count - document A			0
Total word count - document B			8526
Total word count - documents A + B			8526

15/3,AB/27 (Item 25 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00564386
Synthetic lipid A **glycoconjugate antigens** for use in vaccines
Synthetische Lipid-A Clykoconjugate-**Antigene** und deren Verwendung in Impfstoffen
Glycoconjugates synthetiques d'**antigenes** de lipid A et leur utilisation comme vaccins
PATENT ASSIGNEE:
AMERICAN CYANAMID COMPANY, (212594), One Cyanamid Plaza, Wayne, NJ 07470-8426, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;NL;PT;SE)
INVENTOR:
Porro, Massimo, 97 Via Selvapiana, Rapolano Terme, Siena 53040, (IT)
LEGAL REPRESENTATIVE:
Wachtershauser, Gunter, Prof. Dr. (12711), Patentanwalt, Tal 29, 80331 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 570682 A1 931124 (Basic)
EP 570682 B1 970723
APPLICATION (CC, No, Date): EP 93104369 930317;
PRIORITY (CC, No, Date): US 879403 920507
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; NL; PT; SE
INTERNATIONAL PATENT CLASS: C07H-013/04; A61K-039/05; A61K-039/08; A61K-047/48; C07H-015/18;

ABSTRACT EP 570682 A1
Synthetic glycoconjugate antigens of the formula: (see image in original document) for use in vaccines for prophylaxis of septic shock caused by bacterial endotoxin and methods of preparing the glycoconjugates.
ABSTRACT WORD COUNT: 32

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	466
CLAIMS B	(English)	9707W4	405
CLAIMS B	(German)	9707W4	394
CLAIMS B	(French)	9707W4	505
SPEC A	(English)	EPABF1	7685
SPEC B	(English)	9707W4	7440
Total word count - document A			8152

Total word count - document B 8744
Total word count - documents A + B 16896

15/3,AB/28 (Item 26 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00556264
LIGAND GROWTH FACTORS THAT **BIND** TO THE erbB-2 RECEPTOR PROTEIN AND INDUCE CELLULAR RESPONSES
WACHSTUMSFAKTOR-LIGAND, DER AN DEN ERBB-2-REZEPTOR BINDET UND DIE ZELLULAREN REAKTIONEN INDUZIERT
FACTEURS DE CROISSANCE LIGANDS QUI SE LIENT AU RECEPTEUR PROTEIQUE erbB-2 ET INDUISENT DES REPONSES CELLULAIRES
PATENT ASSIGNEE:
GEORGETOWN UNIVERSITY, (210040), 37th and "O" Streets, N.W., Washington, D.C. 20057, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;MC;NL;SE)
INVENTOR:
LIPPMAN, Marc, E., 8004 Herb Farm, Bethesda, MD 20817, (US)
LUPU, Ruth, 1737 Yale Street, Rockville, MD 20850, (US)
LEGAL REPRESENTATIVE:
Dean, John Paul (72772), Withers & Rogers, Goldings House, 2 Hays Lane, London SE1 2HW, (GB)
PATENT (CC, No, Kind, Date): EP 574414 A1 931222 (Basic)
EP 574414 B1 990714
WO 9212174 920723
APPLICATION (CC, No, Date): EP 92903981 920113; WO 92US329 920113
PRIORITY (CC, No, Date): US 640497 910114
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; MC; NL; SE
INTERNATIONAL PATENT CLASS: C07K-014/475; C07K-014/705; C12N-015/12; C12N-005/10; C12N-001/21; C12N-001/38; A61K-038/17; A61K-039/395;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9928	491
CLAIMS B	(German)	9928	502
CLAIMS B	(French)	9928	541
SPEC B	(English)	9928	13436

Total word count - document A 0
Total word count - document B 14970
Total word count - documents A + B 14970

15/3,AB/29 (Item 27 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00556194
NEW INSULIN-LIKE GROWTH FACTOR **BINDING** PROTEIN
INSULINARTIGEN WACHSTUMSFAKTOR BINDENDES PROTEIN
NOUVELLE PROTEINE DE FIXATION DU FACTEUR DE CROISSANCE PROCHE DE L'INSULINE

PATENT ASSIGNEE:
CHIRON CORPORATION, (572531), 4560 Horton Street, Emeryville California 94608-2916, (US), (Proprietor designated states: all)
INVENTOR:
KIEFER, Michael, C., 401 Wright Court, Clayton, MA 94517, (US)
LEGAL REPRESENTATIVE:
Hallybone, Huw George et al (53031), Carpmaels and Ransford, 43 Bloomsbury Square, London WC1A 2RA, (GB)
PATENT (CC, No, Kind, Date): EP 556344 A1 930825 (Basic)
EP 556344 A1 940824
EP 556344 B1 030813
WO 92012243 920723
APPLICATION (CC, No, Date): EP 92903859 920102; WO 92US107 920102
PRIORITY (CC, No, Date): US 638628 910108
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; MC; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/12; C12P-021/08; C12P-021/04; C12N-001/19; C12N-005/10; C12N-015/00; A01K-067/027
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200333	358
CLAIMS B	(German)	200333	340
CLAIMS B	(French)	200333	431
SPEC B	(English)	200333	15707
Total word count - document A			0
Total word count - document B			16836
Total word count - documents A + B			16836

15/3,AB/30 (Item 28 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00539559
Hepatitis B virus **surface proteins** with reduced host carbohydrate content
Hepatitis-B-Virus-Oberflachenproteine mit reduziertem Gehalt an Wirtkohlenwasserstoffen
Proteines de surface du virus de l'hepatitis B presentant des teneurs reduites en hydrates de carbone de l'hote
PATENT ASSIGNEE:
Merck & Co., Inc., (200479), 126, East Lincoln Avenue P.O. Box 2000, Rahway New Jersey 07065-0900, (US), (Proprietor designated states: all)
INVENTOR:
Kniskern, Peter J., 841 Patterson Drive, Lansdale PA 19446, (US)
Hagopian, Arpi, 771 Hartley Drive, Lansdale PA 19446, (US)
LEGAL REPRESENTATIVE:
Thompson, John Dr. et al (62771), Merck & Co., Inc. European Patent Department Terlings Park Eastwick Road, Harlow, Essex CM20 2QR, (GB)
PATENT (CC, No, Kind, Date): EP 516286 A1 921202 (Basic)
EP 516286 B1 020410
APPLICATION (CC, No, Date): EP 92303883 920429;
PRIORITY (CC, No, Date): US 692924 910429

DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12N-015/36; A61K-039/29; C07K-014/02

ABSTRACT EP 516286 A1

In order to produce hepatitis B virus (HBV) surface proteins in the form of particles with substantially reduced entrapped carbohydrate content, DNA encoding the HBV surface proteins was expressed in a recombinant yeast host which is deficient in its ability to glycosylate proteins. These HBV surface proteins display the antigenic sites genetically encoded by the S domain of the HBV virion envelope open reading frame and contains substantially reduced levels of entrapped carbohydrate when compared with HBsAg particles produced in "wild-type" yeast cells. These particles are useful as a vaccine for both the active and passive treatment or prevention of disease and/or infection caused by HBV or other agents serologically related to HBV. (see image in original document)

ABSTRACT WORD COUNT: 120
NOTE:
Figure number on first page: 1

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	305
CLAIMS B	(English)	200215	166
CLAIMS B	(German)	200215	132
CLAIMS B	(French)	200215	201
SPEC A	(English)	EPABF1	10191
SPEC B	(English)	200215	10348
Total word count - document A			10496
Total word count - document B			10847
Total word count - documents A + B			21343

15/3,AB/31 (Item 29 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00539557
Multiple hepatitis B virus **surface proteins** which form particles.
Partikeln bildende multiple Hepatitis-B-Virus-Oberflachen-Proteine.
Proteines multiples de la surface du virus de l'hepatitis B formant des particules.
PATENT ASSIGNEE:
MERCK & CO. INC., (200479), 126, East Lincoln Avenue P.O. Box 2000, Rahway New Jersey 07065-0900, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;PT;SE)
INVENTOR:
Kniskern, Peter J., 841 Patterson Drive, Lansdale, PA 19446, (US)
Hagopian, Arpi, 771 Hartley Drive, Lansdale, PA 19446, (US)
Burke, Pamela, 862 Yorktown Street, Lansdale, PA 19446, (US)
Short, Kathryn R., 582 Forest Road, Wayne, PA 19087, (US)
LEGAL REPRESENTATIVE:
Thompson, John Dr. et al (62771), Merck & Co., Inc. European Patent

Department Terlings Park Eastwick Road, Harlow, Essex CM20 2QR, (GB)
PATENT (CC, No, Kind, Date): EP 511854 A1 921104 (Basic)
APPLICATION (CC, No, Date): EP 92303881 920429;
PRIORITY (CC, No, Date): US 693575 910429
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12N-015/36; A61K-039/29; C07K-015/00;

ABSTRACT EP 511854 A1
In order to produce a mixture hepatitis B virus (HBV) surface proteins in the form of particles, DNA encoding two or more HBV proteins was expressed by a single recombinant yeast. In order to form particles with substantially reduced carbohydrate, such DNA encoding two or more HBV proteins is expressed in a single recombinant yeast host which is deficient in its ability to glycosylate proteins. These HBV proteins display the antigenic sites genetically encoded by the S domain (including the preS domain) of the HBV virion envelope open reading frame and when expressed in a yeast deficient for its ability to glycosylate, contain substantially reduced levels of entrapped carbohydrate when compared with HBsAg particles produced in yeast cells "wild-type" for glycosylation. These particles are useful as a vaccine for both the active and passive treatment or prevention of disease and/or infection caused by HBV or other agents serologically related to HBV including antigenic variants in the immunodominant epitopes of the surface protein and also are useful as antigens and immunogens for development of diagnostic tests for such diseases or infections. (see image in original document)
ABSTRACT WORD COUNT: 187

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	482
SPEC A	(English)	EPABF1	12381
Total word count - document A			12863
Total word count - document B			0
Total word count - documents A + B			12863

15/3,AB/32 (Item 30 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00539303
Cytomodulating **conjugates** of members of specific **binding** pairs
Zytomodulierte Konjugate enthaltend spezifische Bindungspaargliedern
Conjugues cytomodulateurs constants de pair liants specifiques
PATENT ASSIGNEE:
SANGSTAT MEDICAL CORPORATION, (1227840), 1505B Adams Drive, Menlo Park, CA 94025, (US), (Proprietor designated states: all)
INVENTOR:
Pouletty, Philippe, 5 Odell Place, Atherton, California 94025, (US)
LEGAL REPRESENTATIVE:
Stoner, Gerard Patrick et al (59901), MEWBURN ELLIS York House 23 Kingsway, London WC2B 6HP, (GB)
PATENT (CC, No, Kind, Date): EP 510949 A2 921028 (Basic)

EP 510949 A3 921209
EP 510949 B1 970122
EP 510949 B2 030402
APPLICATION (CC, No, Date): EP 92303618 920422;
PRIORITY (CC, No, Date): US 690530 910423
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-047/48

ABSTRACT EP 510949 A2

Novel conjugates are provided comprising a moiety capable of specifically binding to a target cell joined to a selective moiety for binding to an endogenous effector agent, capable of causing cell inactivation or cytotoxicity. Example of conjugates are a ligand for a surface membrane protein, e.g. IL-2 receptor, joined to a polysaccharide A or B antigen. The conjugates may be used to specifically destroy cells associated with a pathogenic condition.

ABSTRACT WORD COUNT: 72

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	392
CLAIMS B	(English)	200314	1081
CLAIMS B	(German)	200314	1079
CLAIMS B	(French)	200314	1165
SPEC A	(English)	EPABF1	3789
SPEC B	(English)	200314	3890
Total word count - document A			4181
Total word count - document B			7215
Total word count - documents A + B			11396

15/3,AB/33 (Item 31 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00533711

Conjugates of the class II protein of the outer membrane of neisseria meningitidis and of HIV-1 related peptides.

Konjugate des Klasse-II-Proteins der ausseren Membran von Neisseria Meningitidis mit HIV-1-verwandten Peptiden.

Conjugues de la proteine classe II de la membrane exterieure de neisseria meningitidis et de peptides associes a HIV-1.

PATENT ASSIGNEE:
MERCK & CO. INC., (200479), 126, East Lincoln Avenue P.O. Box 2000, Rahway New Jersey 07065-0900, (US), (applicant designated states: CH;DE;FR;GB;IT;LI;NL)
INVENTOR:
Emini, A., 6 Faggs Manor Lane, Paoli, PA 19301, (US)
Liu, Margaret A., 4 Cushman Road, Rosemont, PA 19190, (US)
Marburg, Stephen, 50 Concord Avenue, Metuchen, NJ 08840, (US)
Tolman, Richard L., 29 Upper Warren Way, Warren, NJ 07059, (US)
LEGAL REPRESENTATIVE:
Thompson, John Dr. et al (62771), Merck & Co., Inc. European Patent Department Terlings Park Eastwick Road, Harlow, Essex CM20 2QR, (GB)

PATENT (CC, No, Kind, Date): EP 519554 A1 921223 (Basic)
APPLICATION (CC, No, Date): EP 92201693 920611;
PRIORITY (CC, No, Date): US 715273 910619
DESIGNATED STATES: CH; DE; FR; GB; IT; LI; NL
INTERNATIONAL PATENT CLASS: C07K-017/06; C07K-003/28; A61K-039/385; A61K-039/21;

ABSTRACT EP 519554 A1
The Class II major immuno-enhancing protein (MIEP) of Neisseria meningitidis, purified directly from the outer membrane of Neisseria meningitidis, or obtained through recombinant cloning and expression of DNA encoding the MIEP of Neisseria meningitidis, has immunologic carrier as well as immunologic enhancement and mitogenic properties. Conjugates of this protein and HIV-1 related peptides are useful for the induction of mammalian immune responses directed against the peptides, against HIV-1 strains, and for the neutralization of HIV-1 and prevention of HIV-I related diseases.
ABSTRACT WORD COUNT: 83

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	1279
SPEC A	(English)	EPABF1	17403
Total word count - document A			18682
Total word count - document B			0
Total word count - documents A + B			18682

15/3,AB/34 (Item 32 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00473768
The MAC-1 **binding** site of ICAM-1
Die Mac-1-Bindungsstelle von ICAM-1
Le site de liaison d'ICAM-1 pour Mac-1
PATENT ASSIGNEE:
CENTER FOR BLOOD RESEARCH, INC., (1590660), 800 Huntington Avenue, Boston, MA 02115, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Diamond, Michael S., 18 Ware Street No. 2, Cambridge, Massachusetts 02138, (US)
Staunton, Donald E., 124 Chestnut Hill Road, Chestnut Hill, Massachusetts 02167, (US)
Springer, Timothy A., 28 Monadnock Road, Newton, Massachusetts 02157, (US)
LEGAL REPRESENTATIVE:
Laudien, Dieter, Dr. et al (48062), Boehringer Ingelheim Zentrale GmbH ZA Patente Postfach 200, 55216 Ingelheim am Rhein, (DE)
PATENT (CC, No, Kind, Date): EP 488061 A2 920603 (Basic)
EP 488061 A3 920826
EP 488061 B1 981104
APPLICATION (CC, No, Date): EP 91119894 911121;
PRIORITY (CC, No, Date): US 618286 901128

DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C07K-014/705; A61K-038/17; A61K-039/395; C12P-021/08;

ABSTRACT EP 488061 A2
The present invention relates to intercellular adhesion molecules (ICAM-1) and their interaction with the Mac-1 receptor molecule. The invention relates to the use of these molecules and their functional equivalents in the treatment of inflammation and viral diseases.
ABSTRACT WORD COUNT: 40

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9845	214
CLAIMS B	(German)	9845	207
CLAIMS B	(French)	9845	233
SPEC B	(English)	9845	18770
Total word count - document A			0
Total word count - document B			19424
Total word count - documents A + B			19424

15/3,AB/35 (Item 33 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00467209
Improved oligosaccharide **conjugate** vaccines.
Verbesserte Vakzine auf der Basis von Oligosaccharid-Konjugaten.
Vaccins ameliores a base de conjugues d'oligosaccharides.
PATENT ASSIGNEE:
AMERICAN CYANAMID COMPANY, (212594), One Cyanamid Plaza, Wayne, NJ 07470-8426, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;NL;SE)
INVENTOR:
Porro, Massimo, 97 Via Selvapiana, Rapolano Terme, I-53040 Siena, (IT)
LEGAL REPRESENTATIVE:
Wachtershauser, Gunter, Prof. Dr. (12711), Patentanwalt, Tal 29, D-80331 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 477508 A1 920401 (Basic)
EP 477508 B1 950712
APPLICATION (CC, No, Date): EP 91113163 910806;
PRIORITY (CC, No, Date): US 590649 900928
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/09; A61K-031/70;

ABSTRACT EP 477508 A1
The present invention relates to an improved method for producing oligosaccharide conjugate vaccines. In an additional aspect of the invention, oligosaccharide vaccines are produced which elicit a monospecific and homogeneous immune response to capsular polysaccharide. A specific embodiment of the invention provides for vaccines which induce immunity to prevalent serotypes of Streptococcus pneumoniae.
ABSTRACT WORD COUNT: 55

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	383
CLAIMS B	(English)	EPAB95	382
CLAIMS B	(German)	EPAB95	395
CLAIMS B	(French)	EPAB95	409
SPEC A	(English)	EPABF1	8657
SPEC B	(English)	EPAB95	8564
Total word count - document A			9041
Total word count - document B			9750
Total word count - documents A + B			18791

15/3,AB/36 (Item 34 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00462288
Efficacious vaccines against Bordetella pertussis comprising a combination of individually purified pertussis **antigens**.
Wirksame Impfstoffe gegen Bordetella pertussis, die eine Kombination von einzeln gereinigten pertussis **Antigenen** enthalten.
Vaccins efficaces contre Bordetella pertussis comprenant une combinaison d' **antigenes** de pertussis purifies individuellement.
PATENT ASSIGNEE:
AMERICAN CYANAMID COMPANY, (212591), 1937 West Main Street P.O. Box 60, Stamford Connecticut 06904-0060, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;NL;SE)
INVENTOR:
Eckhardt, Thomas G., 69 S.Jackson Avenue, New Windsor, State of New York 12553, (US)
Gotto, John W., 145 1/2 Wayne, Suffern, State of New York 10901, (US)
McClintock, David K., 124 Summit Avenue, Ramsey, State of New Jersey 07446, (US)
Scott, V. Jane, 39 Highland Avenue, Chappaqua, State of New York 10514, (US)
LEGAL REPRESENTATIVE:
Wachtershauser, Gunter, Dr. (12711), Tal 29, W-8000 Munchen 2, (DE)
PATENT (CC, No, Kind, Date): EP 484621 A2 920513 (Basic)
EP 484621 A3 920826
APPLICATION (CC, No, Date): EP 91108108 910518;
PRIORITY (CC, No, Date): US 549236 901107
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/10; A61K-039/295; A61K-039/102;

ABSTRACT EP 484621 A2
This invention is directed to a vaccine for the prevention of disease caused by Bordetella pertussis which comprises the pertussis antigens filamentous hemagglutinin, detoxified lymphocytosis promoting factor and a 69 kilodalton outer membrane protein, where said antigens are individually purified prior to being combined to form the vaccine. The invention is further directed to pertussis vaccines where the antigens are combined in any ratio, including ratios not possible in whole cell or co-purified acellular pertussis vaccines. The pertussis antigens may be further combined with other individually purified pertussis antigens,

pertussis structural components, adjuvants, stabilizers and non-pertussis vaccine components.
ABSTRACT WORD COUNT: 100

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	287
SPEC A	(English)	EPABF1	2983
Total word count - document A			3270
Total word count - document B			0
Total word count - documents A + B			3270

15/3,AB/37 (Item 35 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00409803
COUPLING AGENTS AND STERICALLY HINDERED DISULFIDE **LINKED CONJUGATES** PREPARED THEREFROM.
KUPPLUNGSMITTEL UND STERISCH GEHINDERTE, MIT DISULFID GEBUNDENE KONJUGATE DARAUS.
AGENTS DE COUPLAGE ET CONJUGUES LIES A DES DISULFURES A EMPECHEMENT STERIQUE PREPARES A PARTIR DE TELS AGENTS.
PATENT ASSIGNEE:
CETUS ONCOLOGY CORPORATION, (229563), 1400 Fifty-Third Street, Emeryville California 94608, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;LU;NL;SE)
INVENTOR:
MORELAND, Margaret, 1320 Evelyn Avenue, Berkeley, CA 94702, (US)
GREENFIELD, I., Lawrence, 36 Wildwood Court, Pleasant Hill, CA 94523, (US)
NITECKI, Danute, E., 2296 Virginia Street, Berkeley, CA 94709, (US)
LEGAL REPRESENTATIVE:
Bizley, Richard Edward (28352), HEPWORTH LAWRENCE BRYER & BIZLEY 2nd Floor Gate House South West Gate, Harlow Essex CM20 1JN, (GB)
PATENT (CC, No, Kind, Date): EP 428534 A1 910529 (Basic)
EP 428534 B1 950329
WO 8912624 891228
APPLICATION (CC, No, Date): EP 89907565 890612; WO 89US2546 890612
PRIORITY (CC, No, Date): US 206573 880614
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C07C-323/60; C07C-327/06; C07D-207/46; A61K-039/395; C12P-021/00;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPAB95	1977
CLAIMS B	(German)	EPAB95	1963
CLAIMS B	(French)	EPAB95	2292
SPEC B	(English)	EPAB95	12688
Total word count - document A			0
Total word count - document B			18920

Total word count - documents A + B 18920

15/3,AB/38 (Item 36 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00401822
Conjugate immunogen for aids.
Immunogen-Konjugat gegen Aids.
Conjuges immunogenes contre le Sida.
PATENT ASSIGNEE:
MERCK & CO. INC., (200479), 126, East Lincoln Avenue P.O. Box 2000, Rahway New Jersey 07065-0900, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Emini, Emilio A., 6 Faggs Manor Lane, Paoli, PA 19301, (US)
Marburg, Stephen, 50 Concord Avenue, Metuchen, New Jersey 08840, (US)
Scolnick, Edward M., 811 Wickfield Park Drive, Wynnewood, PA 19096, (US)
Larson, Vivian M., 362 Park Drive, Harleyville PA 19438, (US)
LEGAL REPRESENTATIVE:
Hesketh, Alan, Dr. et al (31763), European Patent Department Merck & Co., Inc. Terlings Park Eastwick Road, Harlow Essex, CM20 2QR, (GB)
PATENT (CC, No, Kind, Date): EP 402088 A2 901212 (Basic)
EP 402088 A3 910306
APPLICATION (CC, No, Date): EP 90306082 900605;
PRIORITY (CC, No, Date): US 362179 890606; US 362178 890606; US 362177 890606; US 362176 890606
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/21; A61K-039/095;

ABSTRACT EP 402088 A2
A conjugate of the major neutralizing determinant of HIV, covalently linked to Neisseria outer membrane proteosome (Omp), is prepared and found to neutralize HIV after inoculation in monkeys. The conjugate is useful as a vaccine against AIDS or ARC as well as in the treatment of AIDS or ARC.
ABSTRACT WORD COUNT: 53

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	1352
SPEC A	(English)	EPABF1	5883
Total word count - document A			7235
Total word count - document B			0
Total word count - documents A + B			7235

15/3,AB/39 (Item 37 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00389163
Use of intercellular adhesion molecules, and their **binding** ligands in the treatment of asthma.

Verwendung von interzellularen Adhasions-Molekulen und deren Bindungsliganden bei der Behandlung von Asthma.
Utilisation des molecules d'adhesion intercellulaire et leurs ligands de liaison dans le traitement de l'asthme.
PATENT ASSIGNEE:
Boehringer Ingelheim Pharmaceuticals Inc., (716270), 90 East Ridge P.O. Box 368, Ridgefield Connecticut 06877, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Wegner, Craig D., 10 Skyview Drive, New Milford Connecticut 06766, (US)
Gundel, Robert H., RR2 Box 74 Hurds Corner Road, Pawling New York 12564, (US)
Rothlein, Robert, 32 Tamanny Trail, Danbury Connecticut 06811, (US)
LEGAL REPRESENTATIVE:
Laudien, Dieter, Dr. et al (48063), Boehringer Ingelheim GmbH, Abteilung Patente, W-6507 Ingelheim am Rhein, (DE)
PATENT (CC, No, Kind, Date): EP 387701 A1 900919 (Basic)
EP 387701 B1 920812
APPLICATION (CC, No, Date): EP 90104423 900308;
PRIORITY (CC, No, Date): US 321018 890309; US 321239 890309; US 321237 890309; US 324481 890316; US 401409 890901
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-037/02; A61K-039/395;

ABSTRACT EP 387701 A1
The present invention relates to the use of intercellular adhesion molecules (ICAM-1), their functional derivatives, and molecules which bind to them, in the treatment of asthma.
ABSTRACT WORD COUNT: 30

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	517
CLAIMS B	(German)	EPBBF1	529
CLAIMS B	(French)	EPBBF1	566
SPEC B	(English)	EPBBF1	12664
Total word count - document A			0
Total word count - document B			14276
Total word count - documents A + B			14276

15/3,AB/40 (Item 38 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00389051
Intercellular adhesion molecule - 2 and its **binding** ligands
Interzellulares Adhasions-Molekul-2 und seine Bindungsliganden
Molecule d'adhesion intercellulaire-2 et ses ligands de liaisons
PATENT ASSIGNEE:
CENTER FOR BLOOD RESEARCH, INC., (1590660), 800 Huntington Avenue, Boston, MA 02115, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Springer, Timothy Alan, 28 Monadnock Road, Chestnut Hill, MA 02167, (US)

Dustin, Michael Loran, 231 Park Drive No. 23, Boston, MA 02215, (US)
Staunton, Donald E., 124 Chestnut Hill Road, Chestnut Hill, MA 02167, (US)
LEGAL REPRESENTATIVE:
Laudien, Dieter, Dr. et al (48061), Boehringer Ingelheim International GmbH ZA Patente Postfach 200, 55216 Ingelheim am Rhein, (DE)
PATENT (CC, No, Kind, Date): EP 387668 A1 900919 (Basic)
EP 387668 B1 961211
APPLICATION (CC, No, Date): EP 90104295 900307;
PRIORITY (CC, No, Date): US 321238 890309; US 454294 891222
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/12; C07K-014/435; C07K-016/18; C12P-021/00; C12P-021/08; A61K-039/395; A61K-038/17; C12Q-001/68; A61K-045/06;

ABSTRACT EP 387668 A1
The present invention relates to intercellular adhesion molecules (ICAM-2) which are involved in the process through which lymphocytes recognize and migrate to sites of inflammation as well as attach to cellular substrates during inflammation. The invention is directed toward such molecules, screening assays for identifying such molecules and antibodies capable of binding such molecules. The invention also includes uses for adhesion molecules and for the antibodies that are capable of binding them.
ABSTRACT WORD COUNT: 76

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	768
CLAIMS B	(English)	EPAB96	1401
CLAIMS B	(German)	EPAB96	1294
CLAIMS B	(French)	EPAB96	1500
SPEC A	(English)	EPABF1	13701
SPEC B	(English)	EPAB96	13467
Total word count - document A			14471
Total word count - document B			17662
Total word count - documents A + B			32133

15/3,AB/41 (Item 39 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00384471
T-CELL EPITOPE AS CARRIERS MOLECULE FOR **CONJUGATE** VACCINES.
T-ZELLEN-EPITOPE ALS TRAGER FUR EINEN KONJUGIERTEN IMPFSTOFF.
EPITOPES DE CELLULES T A TITRE DE MOLECULES PORTEUSES POUR VACCINS CONJUGUES.
PATENT ASSIGNEE:
PRAXIS BIOLOGICS, INC., (693521), 30 Corporate Woods, Rochester New York 14623, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;LU;NL;SE)
INVENTOR:
BIXLER, Garvin, 92 Squirrel's Heath Road, Fairport, NY 11450, (US)
PILLAI, Subramonia, 286 Vollmer Parkway, Rochester, NY 14623, (US)

INSEL, Richard, 167 Oakdale Drive, Rochester, NY 14618, (US)
LEGAL REPRESENTATIVE:
Allam, Peter Clerk et al (27601), LLOYD WISE, TREGEAR & CO. Norman House 105-109 Strand, London WC2R 0AE, (GB)
PATENT (CC, No, Kind, Date): EP 399001 A1 901128 (Basic)
EP 399001 B1 940727
WO 8906974 890810
APPLICATION (CC, No, Date): EP 89908669 890131; WO 89US388 890131
PRIORITY (CC, No, Date): US 150688 880201
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/385; C07K-015/04; A61K-039/155;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	747
CLAIMS B	(German)	EPBBF1	655
CLAIMS B	(French)	EPBBF1	800
SPEC B	(English)	EPBBF1	13397
Total word count - document A			0
Total word count - document B			15599
Total word count - documents A + B			15599

15/3,AB/42 (Item 40 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00382662
CONJUGATION OF POLYMER TO COLONY STIMULATING FACTOR-1.
KONJUGATION DER POLYMERE AN KOLONIEN STIMULIERENDEN FAKTOR.
CONJUGAISON D'UN POLYMERE AVEC LA PROTEINE CSF-1.
PATENT ASSIGNEE:
CETUS ONCOLOGY CORPORATION, (229563), 1400 Fifty-Third Street, Emeryville California 94608, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;LU;NL;SE)
INVENTOR:
SHADLE, Paula, J., 5110 MacDonald Avenue, Richmond, CA 94805, (US)
KOTHS, Kirston, E., 2646 Mira Vista Drive, El Cerrito, CA 94530, (US)
MORELAND, Margaret, 1320 Evelyn Avenue, Berkeley, CA 94702, (US)
KATRE, Nandini, 6107 Jordan Avenue, El Cerrito, CA 94530, (US)
LAIRD, Walter, J., 2660 Lassen Way, Pinole, CA 94564, (US)
ALDWIN, Lois, 179 Lakeshore Drive, San Mateo, CA 94402, (US)
NITECKI, Danute, E., 2296 Virginia Street, Berkeley, CA 94709, (US)
YOUNG, John, D., 1430 Piedra Drive, Walnut Creek, CA 94596, (US)
LEGAL REPRESENTATIVE:
Bizley, Richard Edward et al (28353), HEPWORTH, LAWRENCE BRYER & BIZLEY 2nd Floor Gate House South West Gate, Harlow Essex CM20 1JN, (GB)
PATENT (CC, No, Kind, Date): EP 402378 A1 901219 (Basic)
EP 402378 B1 940302
WO 8906546 890727
APPLICATION (CC, No, Date): EP 89902670 890123; WO 89US270 890123
PRIORITY (CC, No, Date): US 146275 880120
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-047/00; A61K-037/02;

NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	1119
CLAIMS B	(German)	EPBBF1	1078
CLAIMS B	(French)	EPBBF1	1211
SPEC B	(English)	EPBBF1	15788
Total word count - document A			0
Total word count - document B			19196
Total word count - documents A + B			19196

15/3,AB/43 (Item 41 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00358266
Recombinant methods for the production of ricin a, ricin b, ricin or diphtheria **toxin** (dt)a or ab' fragment, suitable hosts and vectors therefor, and **conjugates**
Rekombinante Verfahren fur die Herstellung von Ricin-A, Ricin-B, Ricin oder Diphterietoxin-A oder AB'-Fragment, Wirte und Vektoren dafur und Konjugate, die Rici
Methodes recombinantes pour la production de ricine A, ricine B, ricine ou de fragment A ou AB' de la **toxine** diphterique, hotes et vecteurs a cet effet et conju
PATENT ASSIGNEE:
CETUS CORPORATION, (229561), 1400 Fifty-Third Street, Emeryville California 94608, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;LI;LU;NL;SE)
INVENTOR:
Gelfand, David, 6208 Chelton Drive, Oakland California 94611, (US)
Lawyer, Frances Cook, 6641 Saroni Drive, Oakland California 94611, (US)
Horn, Glenn, 3 Admiral Drive No. F370, Emeryville California 94608, (US)
Greenfield, Lawrence, 555 Pierce Street Unit 435, Albany California 94706, (US)
Nitecki, Danute, 2296 Virginia Street, Berkeley California 94709, (US)
Kaplan, Donald, 3301 Noeske Drive, Midland Michigan 48640, (US)
Piatak, Michael, Jr., 1120 Alfred Avenue, Walnut Creek California 94596, (US)
LEGAL REPRESENTATIVE:
Lawrence, Malcolm Graham et al (47876), Hepworth Lawrence & Bryer 15th floor Terminus House Terminus Street, Harlow Essex CM20 1XD, (GB)
PATENT (CC, No, Kind, Date): EP 335476 A2 891004 (Basic)
EP 335476 A3 891213
APPLICATION (CC, No, Date): EP 89201162 850207;
PRIORITY (CC, No, Date): US 578115 840208; US 587121 840208; US 578122 840209; US 648759 840907; US 653515 840920
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; LI; LU; NL; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 170697
INTERNATIONAL PATENT CLASS: C12N-015/00; C12P-021/00;

ABSTRACT EP 335476 A2

Recombinant methods for the production of Ricin A, Ricin B, Ricin of Diphtheria toxin (DT)A or AB(min) fragment are described together with suitable hosts and vectors. Immunotoxin conjugates comprising Ricin toxin A chain or Diphtheria toxin are also described.
ABSTRACT WORD COUNT: 43

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	301
SPEC A	(English)	EPABF1	22059
Total word count - document A			22360
Total word count - document B			0
Total word count - documents A + B			22360

15/3,AB/44 (Item 42 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00339312
Haemophilus influenzae type B polysaccharide-**outer membrane protein conjugate** vaccine.
Haemophilus influenzae Typ B Polysaccharid-Aussermembranprotein-Konjugat als Impfstoff.
Vaccin a base d'un **conjugat** de proteine de membrane externe et de polysaccharide de type B d'haemophilus influenzae.
PATENT ASSIGNEE:
AMERICAN CYANAMID COMPANY, (212594), One Cyanamid Plaza, Wayne, NJ 07470-8426, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;NL;SE)
INVENTOR:
Kuo, Joseph S.-C., 67 Constitution Drive, Tappan, NY 10983, (US)
Bristol, James Edwin, 58 North Serven Street, Pearl River, NY 10965, (US)
LEGAL REPRESENTATIVE:
Wachtershauser, Gunter, Dr. (12711), Tal 29, D-80331 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 338265 A2 891025 (Basic)
EP 338265 A3 891213
EP 338265 B1 940504
APPLICATION (CC, No, Date): EP 89104996 890321;
PRIORITY (CC, No, Date): US 183206 880419
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/102;

ABSTRACT EP 338265 A2
Immunogenic conjugates of a 38,000 daltons or 40,000 daltons outer membrane protein of H. Influenzae type b and oxidized polyribosyl-ribitol-phosphate polysaccharide fragments of H. influenzae type b are disclosed. Vaccines containing the conjugates are disclosed as useful in immunizing against H. Influenzae type b caused disease. Methods for isolating and purifying the 38,000 daltons and 40,000 daltons outer membrane proteins and for preparing the oxidized polyribosyl-ribitol-phosphate polysaccharide fragments are also disclosed.
ABSTRACT WORD COUNT: 75

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPBBF1	715
CLAIMS B	(English)	EPBBF1	975
CLAIMS B	(German)	EPBBF1	893
CLAIMS B	(French)	EPBBF1	1183
SPEC A	(English)	EPBBF1	6020
SPEC B	(English)	EPBBF1	5924
Total word count - document A			6735
Total word count - document B			8975
Total word count - documents A + B			15710

15/3,AB/45 (Item 43 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00308504
Non-immunochemical **binding** of **lipopolysaccharides** and sandwich essays therefore.
Nichtimmunochemische Bindung von **Lipopolysacchariden** und Sandwich-Bestimmung dafur.
Fixation non immunochimique de **lipopolysaccharides** et essais sandwichs a cet effet.
PATENT ASSIGNEE:
E.I. DU PONT DE NEMOURS AND COMPANY, (200580), 1007 Market Street, Wilmington Delaware 19898, (US), (applicant designated states: DE;FR;GB;IT;NL)
INVENTOR:
Connelly, Mark Carle, 22 E. 4th Street, New Castle, DE 19720, (US)
LEGAL REPRESENTATIVE:
Myerscough, Philip Boyd et al (34221), J.A.Kemp & Co. 14, South Square Gray's Inn, London, WC1R 5EU, (GB)
PATENT (CC, No, Kind, Date): EP 279517 A1 880824 (Basic)
EP 279517 B1 911127
APPLICATION (CC, No, Date): EP 88300450 880120;
PRIORITY (CC, No, Date): US 11327 870121
DESIGNATED STATES: DE; FR; GB; IT; NL
INTERNATIONAL PATENT CLASS: G01N-033/53; G01N-033/543; G01N-033/579; G01N-033/569; G01N-033/571

ABSTRACT EP 279517 A1
Sandwich assays for detecting and identifying lipopolysaccharides of gram negative bacteria utilizing immobilized lipopolysaccharide binding proteins and labelled detection reagents are provided. The active supports are also useful in removing LPS from biomedical and cosmetic preparations.
ABSTRACT WORD COUNT: 40

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	492
CLAIMS B	(German)	EPBBF1	268
CLAIMS B	(French)	EPBBF1	327

SPEC B	(English)	EPBBF1	5762
Total word count - document A			0
Total word count - document B			6849
Total word count - documents A + B			6849

15/3,AB/46 (Item 44 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00267640
Method for producing hepatitis B virus core **antigen** (HBcAg) in yeast.
Verfahren zur Herstellung von Hepatitis-B-Virus-**Innenkorperantigen** (HBcAg) in Hefe.
Procede de production d'**antigene** du noyau du virus de l'hepatite B (HBcAg) dans la levure.
PATENT ASSIGNEE:
MERCK & CO. INC., (200479), 126, East Lincoln Avenue P.O. Box 2000, Rahway New Jersey 07065-0900, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;IT;LI;LU;NL;SE)
INVENTOR:
Ellis, Ronald W., 1407 Edgevale Road, Overbrook Hills Pennsylvania 19440, (US)
Hagopian, Arpi, 771 Hartley Drive, Lansdale Pennsylvania 19446, (US)
Kniskern, Peter J., 841 Patterson Drive, Lansdale Pennsylvania 19446, (US)
LEGAL REPRESENTATIVE:
Cole, William Gwyn (29438), European Patent Department, Merck & Co., Inc., Terlings Park, Eastwick Road, Harlow, Essex CM20 2QR, (GB)
PATENT (CC, No, Kind, Date): EP 251460 A2 880107 (Basic)
EP 251460 A3 880720
EP 251460 B1 920812
APPLICATION (CC, No, Date): EP 87304314 870515;
PRIORITY (CC, No, Date): US 866558 860523
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/51; C12N-001/16; A61K-039/29;

ABSTRACT EP 251460 A2
Hepatitis B virus core antigen (HBcAg) has been expressed in yeast at levels approaching 30% of the soluble yeast proteins. The expressed 22,000 dalton polypeptide aggregates into 28 nm particles which are morphologically and immunologically indistinguishable from native HBcAg particles. This protein is useful in in vitro diagnostic systems and in vaccines for treatment and prevention of hepatitis B virus-induced diseases and/or infections.
ABSTRACT WORD COUNT: 67

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	263
CLAIMS B	(German)	EPBBF1	157
CLAIMS B	(French)	EPBBF1	200
SPEC B	(English)	EPBBF1	2619
Total word count - document A			0
Total word count - document B			3239

Searcher : Shears 571-272-2528

Total word count - documents A + B 3239

15/3,AB/47 (Item 45 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00248810
T and B cell epitopes of the pre-S region of hepatitis B virus surface **antigen.**
T- und B-Zellepitopen des pre-S-Gebietes des Hepatitis-B-**Oberflachenantigens.**
Epitopes de cellules T et B de la region pre-S de l'**antigene** de surface de l'hepatite B.
PATENT ASSIGNEE:
SCRIPPS CLINIC AND RESEARCH FOUNDATION, (255640), 10666 North Torrey Pines Road, La Jolla California 92037, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Millich, David R., 11591 Polaris, Mica Mesa California 92126, (US)
Thornton, George B., 11039 Matinal Circle, San Diego California 92127, (US)
LEGAL REPRESENTATIVE:
Fisher, Adrian John et al , CARPMAELS & RANSFORD 43 Bloomsbury Square, London WC1A 2RA, (GB)
PATENT (CC, No, Kind, Date): EP 250253 A2 871223 (Basic)
EP 250253 A3 890322
APPLICATION (CC, No, Date): EP 87305452 870619;
PRIORITY (CC, No, Date): US 877020 860620; US 60214 870610
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C07K-007/00; A61K-039/29;

ABSTRACT EP 250253 A2
Polypeptides corresponding in amino acid residue sequence to T and B cell epitopes in the pre-S region of HBsAg are disclosed. A method of mitigating nonresponsiveness to an HBV vaccine comprising operatively linking a pre-S1 region T cell epitope to the immunogen of the vaccine is also disclosed.
ABSTRACT WORD COUNT: 52

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	692
SPEC A	(English)	EPABF1	23137
Total word count - document A			23829
Total word count - document B			0
Total word count - documents A + B			23829

15/3,AB/48 (Item 46 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00191227
TOXIN CONJUGATES.

TOXINKONJUGATE.
CONJUGUES DE TOXINES.
PATENT ASSIGNEE:
CETUS CORPORATION, (229561), 1400 Fifty-Third Street, Emeryville California 94608, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;LI;LU;NL;SE)
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Bizley, Richard Edward et al (28352), HEPWORTH LAWRENCE BRYER & BIZLEY 2nd Floor Gate House South West Gate, Harlow, Essex CM20 1JN, (GB)
PATENT (CC, No, Kind, Date): EP 170697 A1 860212 (Basic)
EP 170697 B1 911023
WO 8503508 850815
APPLICATION (CC, No, Date): EP 85901197 850207; WO 85US197 850207
PRIORITY (CC, No, Date): US 578115 840208; US 587121 840208; US 578122 840209; US 648759 840907; US 653515 840920
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/44; A61K-047/48; C07K-017/06; C12N-015/11; C12N-015/29;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	329
CLAIMS B	(German)	EPBBF1	319
CLAIMS B	(French)	EPBBF1	383
SPEC B	(English)	EPBBF1	14749
Total word count - document A			0
Total word count - document B			15780
Total word count - documents A + B			15780

15/3,AB/49 (Item 47 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00118135
SYNTHETIC PICORNAVIRUS **ANTIGEN.**
KUNSTLICHES **PIKORNAVIRUSANTIGEN.**
ANTIGENE SYNTHETIQUE DU PICORNAVIRUS.
PATENT ASSIGNEE:
BITTLE, James L., (357570), 5353 Calle Vista, San Diego CA 92109, (US), (applicant designated states: AT;BE;DE;FR;GB;NL;SE)
LERNER, Richard A., (357580), 7750 East Roseland, La Jolla CA 92037, (US), (applicant designated states: AT;BE;DE;FR;GB;NL;SE)
INVENTOR:
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LERNER, Richard A., 7750 East Roseland, La Jolla CA 92037, (US)
LEGAL REPRESENTATIVE:
Fisher, Adrian John et al (52611), CARPMAELS & RANSFORD 43 Bloomsbury Square, London WC1A 2RA, (GB)
PATENT (CC, No, Kind, Date): EP 105346 A1 840418 (Basic)
EP 105346 A1 880113
EP 105346 B1 911113
WO 8303547 831027
APPLICATION (CC, No, Date): EP 83901543 830406; WO 83US477 830406
PRIORITY (CC, No, Date): US 368308 820414; US 478847 830325
DESIGNATED STATES: AT; BE; DE; FR; GB; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/125; A61K-039/13; A61K-039/135; G01N-033/541; G01N-033/561;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	4323
CLAIMS B	(German)	EPBBF1	4318
CLAIMS B	(French)	EPBBF1	4508
SPEC B	(English)	EPBBF1	12733
Total word count - document A			0
Total word count - document B			25882
Total word count - documents A + B			25882

-Author (s)

Set	Items	Description
S18	19	AU=(ATUMUGHAM, R? OR ATUMUGHAM R? OR ARUMUGHAM, R? OR ARUMUGHAM R?)
S19	77	AU=(FORTUNA NEVIN, M? OR FORTUNA NEVIN M? OR NEVIN FORTUNA M? OR NEVIN FORTUNA, M? OR NEVIN, M? OR NEVIN M? OR FORTUNA, M? OR FORTUNA M?)
S20	301	AU=(APICELLA, M? OR APICELLA M?)
S21	1442	AU=(GIBSON, B? OR GIBSON B?)
S22	1	S18 AND S19 AND S20 AND S21
S23	3	S18 AND (S19 OR S20 OR S21)
S24	1	S19 AND (S20 OR S21)
S25	65	S20 AND S21
S26	2	(S18 OR S19 OR S20 OR S21 OR S25) AND (S4 OR S5)
S27	3	(S22 OR S23 OR S24 OR S26) NOT (S12 OR S15)
S28	2	RD (unique items)

>>>No matching display code(s) found in file(s): 65, 113

28/3,AB/1 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00864761
NON-TOXIC MUTANTS OF PATHOGENIC GRAM-NEGATIVE BACTERIA
NICHTTOXISCHE MUTANTEN PATHOGENER GRAM-NEGATIVER BAKTERIEN
MUTANTS NON TOXIQUES DE BACTERIES PATHOGENES GRAM-NEGATIVES
PATENT ASSIGNEE:
UNIVERSITY OF IOWA RESEARCH FOUNDATION, (384488), Oakdale Research Center, 100 Oakdale Campus No. 214 TIC, Iowa City, IA 52242-5000, (US), (applicant designated states:

AT;BE;CH;DE;DK;ES;FI;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
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PATENT (CC, No, Kind, Date): EP 876150 A1 981111 (Basic)
WO 9719688 970605
APPLICATION (CC, No, Date): EP 96942080 961127; WO 96US18984 961127
PRIORITY (CC, No, Date): US 565943 951201
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-035/66; A61K-039/00; A61K-039/02; C07K-014/195;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English

28/3,AB/2 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0213845 DBR Accession No.: 97-08966 PATENT
New Gram-negative bacterial pathogen vaccines - Gram-negative bacterium htrB endotoxin gene mutagenesis for reduced toxicity and use as a vaccine
AUTHOR: **Apicella M A**; Sunshine M G; Lee N G; **Arumugham R**; **Gibson B W**
CORPORATE SOURCE: Iowa City, IA, USA; Oakland, CA, USA; Madison, NJ, USA.
PATENT ASSIGNEE: Univ.Iowa-Res.Found.; Univ.California; American-Cyanamid 1997
PATENT NUMBER: WO 9719688 PATENT DATE: 970605 WPI ACCESSION NO.: 97-310355 (9728)
PRIORITY APPLIC. NO.: US 565943 APPLIC. DATE: 951201
NATIONAL APPLIC. NO.: WO 96US18984 APPLIC. DATE: 961127
LANGUAGE: English
ABSTRACT: A method for immunizing an individual to prevent disease caused by a Gram-negative bacterial pathogen is claimed, which involves vaccinating the individual with a formulation (claimed) consisting of a Gram-negative bacterium htrB mutant, endotoxin isolated from the mutant, endotoxin isolated from the mutant and conjugated with a carrier protein, or a mutant which has been genetically engineered to express at least one heterologous vaccine antigen as the active

ingredient. Also claimed are methods for producing a mutant endotoxin or a Gram-negative bacterium mutant having substantially reduced toxicity as compared with the wild-type endotoxin or bacterium, which involves mutating an htrB gene within the bacterium causing a phenotype characterized by a mutant endotoxin lacking at least one secondary acyl chain on lipid-A contained in the wild-type bacterium. The endotoxins have reduced toxicity compared with the wild-type endotoxins and yet retain antigenicity. The compositions can be used as prophylactic or therapeutic vaccines against endotoxic shock and Gram-negative bacteremia. (79pp)

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